The Study of Planarized and Planar Cyclohexane Rings on the Basis of Molecular Mechanics

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Recent rapid development of synthetic and theoretical methods has yielded molecules with unusual stereochemistry on carbon atom. One of the most interesting examples of such earlier unsought of arrangements is provided by planar cyclohexane rings. Few molecules of this kind have been synthesized and two others have been postulated on the basis of molecular mechanics calculations. In the present article a critical review of existing experimental and theoretical results is supplemented with a molecular mechanics study of a series of cyclohexanes fused with up to six 3-, 4-, and 5-membered rings causing the flattening of C_6 ring. The existing experimental data and the results of the calculations seem to indicate that the flattening is more pronounced when smaller and/or larger number of rings are fused. The applicability and limitations of molecular mechanics with the MM2 parameterization to the study of the flattening of cyclohexane ring have been critically analyzed. The synthetic efforts in this field seem to indicate that some results calculated for hypothetical molecules will be checked in the near future. Similarly to hypothetical [6]asterane and hexaprismane, the planarity of [6.3]coronane has been postulated.

Until recently, the following stable conformations of a cyclohexane ring has been taken into account: chair, twist, boat (and half-chair for a ring with a double bond). In their review on the nonchair conformations of cyclohexane rings published in 1974 Kellie and Riddell[1] limited themselves with the former three conformations. The half-chair and boat rings have been also lately discussed by Vereshchagin.[2] Due to a rapid development of synthetic and theoretical methods in the last 15 years molecules with considerable distortions from a standard cyclohexane geometry toward a planar cyclohexane ring or even those with completely planar rings have been reported. Several derivatives of *cis*- and *trans*-tris-σ-homobenzenes (**1**—**3**, complexes of **4**) have been found to exhibit planar sixmembered rings by means of X-ray analysis.[3-6] *trans*-Tris-σ-homobenzene **5** has been synthesized by Engelhardt and Lüttke.[7] The authors claimed that the central ring in the molecule is planar but no sound arguments in favor of the planarity have been given. A highly strained diplanar structure of hexamethylated derivative **6** with the torsional angle between the planes close to 180°[8] seems to validate the planarity of the parent molecule **5**. Planar C_6 rings have been also postulated for other types of hypothetical molecules by Osawa and Musso **7**[9] and Allinger and Eaton **8**[10] on the basis of molecular mechanics calculations.

Molecules with flattened but not completely planar cyclohexane rings are much more common. A *cis*-fusion of a 4- or 5-membered ring in **9** and **10**[11,12] was reported to yield a distorted C_6 ring with a flattening along the junction and an enhanced twisting in the other part of the ring and a fusion with cyclopropane is known to result in a half-chair conformation.[2,13] The overall flattening effect of a cis-fusion can be estimated by means of a sum of the absolute values of torsional angles within the C_6 ring α. The lowering of the α value from the cyclohexane value of 336°[14] is small for bicyclo[4.3.0]nonane (**9**), it increases for bicyclo[4.2.0]octane (**10**) and is the biggest for bicyclo[4.1.0]heptane (**11**) where the six-membered ring assumes a half-chair conformation (the corresponding values are given in Table 1). A cis-substitution of subsequent small rings seem to cause further flatten-

Table 1. The Calculated Steric Energies, Heats of Formation (in kcal mol^{-1}) and α Values and the Corresponding Experimental Data

Molecule	E_s	HOF	α calcd degrees	α exp. degrees
9[a]	18.3	−30.5 calcd −30.4 exp.[j]	317.6	314.0[b]
10	36.6	−5.7 calcd −6.4 exp.[j]	280.6	280.6[c]
11	16.6	1.2 calcd 0.4 exp.[d]	203.8	
cis-**13**[e]	27.1	29.6	153.3	
trans-**13**[e]	24.6	27.1	116.9	
cis-**5**	39.8	57.5[i]	7.8	
trans-**5**	36.3	54.0	15.8	
trans-**6**	55.6	20.8	58.6	f)
14	82.9	−20.1	201.0	
15	161.1	90.2	144.4	163.3[g]
16	98.9	−18.5	236.2	
17	193.2	114.4	135.9	
18	77.8	161.0	34.8	
19	100.0	215.6	0.1	
21	95.5	−24.9	238.5	256.8[h]

a) For the less stable *cis*-isomer studied in this work. b) Ref. 11. c) Ref. 12. d) Ref. 21. e) Favoured conformer with H(1) and H(2) in diequatorial disposition for *trans*-**13**. The experimental data of Ref. 17 are insufficient for α determination. See text for discussion of the α value. f) As above, the experimental data of Ref. 8 are insufficient for the α determination. See text for discussion of the α value. g) The experimental value refers to 13-(3,5-dinitrobenzoyloxy)hexacyclo-[12.2.0.0^{1,4}.0^{4,7}.0^{7,10}.0^{10,13}]hexadecane (**22**) reported in Ref. 18. h) The experimental value refers to the analogous compound **20**.[19] i) A MINDO/3 value of 52.7 kcal mol^{-1} has been reported.[32] j) Ref. 31.

ing of the ring under investigation. Examples of this type include several derivatives of *cis*- and *trans*-tricyclo[5.1.0.0^{3,5}]octanes (**12**) and those of *cis*- and *trans*-tricyclo[5.1.0.0^{2,4}]octanes (**13**).[2,15–17]

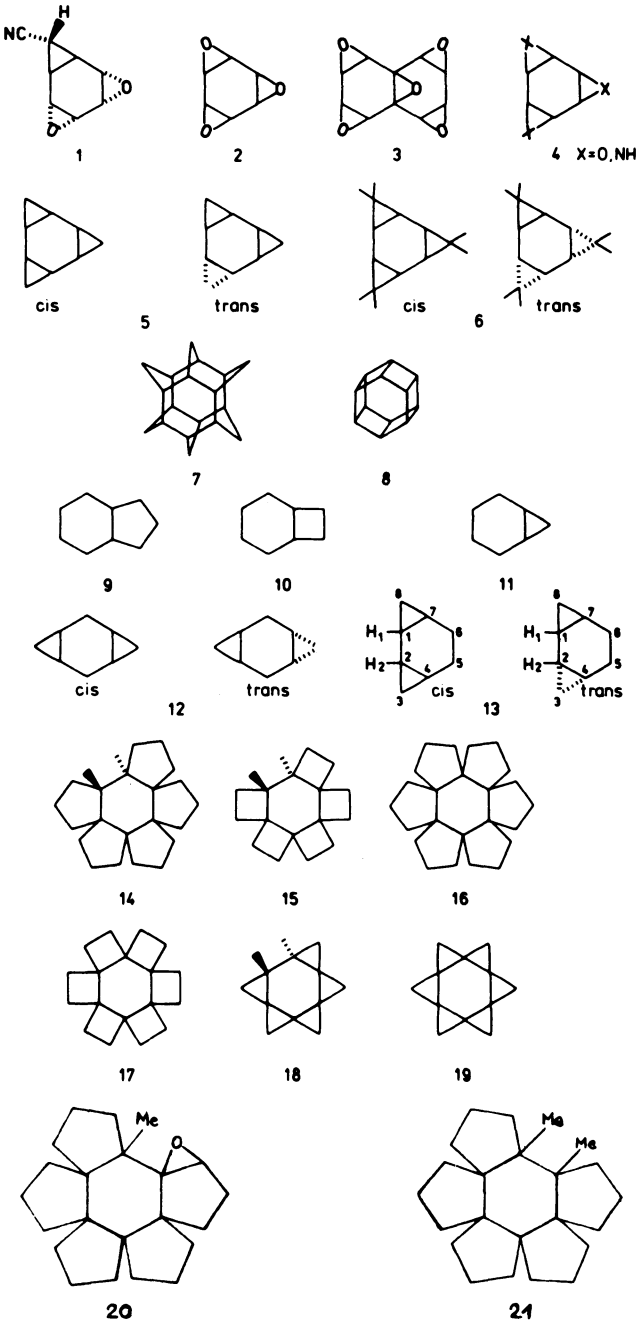
Recent elegant syntheses carried out by Fitjer and coworkers[18,19] yielded derivatives of polycycles **14** and **15** (exhibiting a considerable flattening of the C_6 rings) with the purpose to obtain the corresponding coronanes **16** and **17**.

Some molecular mechanics[20] studies of the molecules under investigation have been reported but they are inconsistent and deal only with some particular aspects. Boyd and coworkers[21] calculated thermochemical properties of a series of bicyclic molecules using their own force field. They have reported the calculated values of bond angles and torsional angles for the molecules **9**—**11** but, having no experimental data to compare with, they did not discuss the geometrical results obtained. In their electron diffraction study of *cis*- and *trans*-bicyclo[4.3.0]nonanes (**9**) Enden and Geise[11] repeated the molecular mechanics calculations for the molecules using the force field proposed by Ermer and Lifson.[22] Spelbos et al. repeated[12] the Boyd force field calculations similarly, in addition to their electron diffraction study of *cis*- and *trans*-fused bicyclo[4.2.0]octanes. An old diffraction work on bicyclo[4.1.0]heptane (**11**) has also been accompanied by simplified molecular mechanics calculations using still another force field.[13]

Heat of formation values (HOF) for **9** and **10** have been also calculated by Allinger[24] using his MM2 parameterisation[23] and the MM2 calculations for **11** has been only cited as unpublished results.[25] The same force field used by Osawa and coworkers[26] for tricyclic systems *cis*- and *trans*-**13** yielded results somewhat different from these reported in the present paper. They will be discussed below in some detail.

The aim of this work was to analyze by means of molecular mechanics[20] with the MM2 parameterization[23] the flattening of cyclohexane ring forced by *cis*-fusion of small ring(s) to find out regularities and to check the applicability of the method to the study of this interesting problem. For the sake of completeness the following series of molecules has been studied: **9**—**11**, *cis*- and *trans*-**13**, *cis*- and *trans*-**5**, *tarans*-**6**, **14**—**19**, and **21**. *cis*- and *trans*-tricyclo[5.1.0.0^{3,5}]octanes (**12**) have not been included into the series in view of the unreliability of one parameter involved in the calculations which will be discussed below.

The available experimental data and the results of the calculations carried out in the present work seem to indicate that *cis*-fusion of a small ring flattens cyclohexane ring and the flattening is more pronounced when more and smaller rings are involved in fusion with the C_6 ring. In the limiting case of *cis*- and *trans*-tris-σ-homobenzenes (**5**) and that of the hypothetical [6.3]coronane (**19**) the cyclohexane ring is completely planar. The calculations yielded also the HOF values



for the molecules under investigation.

Method

The calculations have been carried out using MM2-type program KNOW[27] on Mera 400 computer with the standard MM2 parameterization.[23] The molecules *cis*- and *trans*-**5**, *trans*-**6**, *cis*- and trans-**13**, **14**—**19**, and **21** represent highly strained systems for which the method could be of limited accuracy[28,29] or even fail since minor inaccuracies in potential functions and/or parameters used, which do not impair results for less congested molecules, can influence them for highly strained systems. Therefore, the calculations are also of value for detection of deficiencies and limitations of

the method itself. The problem is further complicated by the fact that the corresponding experimental data to compare with are scarce and the ones at our disposal often refer to solid state X-ray of derivatives of the molecules under investigation. In cases when such a comparison could be carried out (*trans*-**6**, **13**—**15**, **20**, **21**)† the results of the calculations performed in the present work seem to indicate that (1) the method yields reliable estimation of torsional angles (see Tables and discussion below) and, therefore, seems suitable for the analysis of planarity of cyclohexane ring. (2) On the other hand, it performs badly for bond lengths in highly congested systems. In particular, contrary to the report by Osawa et al.[26] we were not able to reproduce the bond lengths for *cis*- and *trans*-**13**.†† Consequently, (3) poor reproducibility of bond lengths and the condition for ring closure lead to wrong values of bond angles. Therefore, the calculations reported here seem to underline the need for further refinement of the MM2 force field parameters involving cyclopropane ring. On the other hand, the magnitude of the V_3 torsional constant of the type 22-22-1-22 chosen in Ref. 25 raises more serious objections. The value of 4.5 kcal mol^{-1} assigned to this constant in the MM2 parameterization has been questioned by Rüchardt et al.[28] We also believe that this value is unreliable since it is about 10 times bigger than other constants of similar type. Thus, as stated above, the lack of this constant precluded the performance of the calculations for the *cis*- and *trans*-tricyclo[5.1.0.0^{3,5}]octanes (**12**).

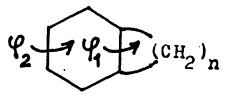
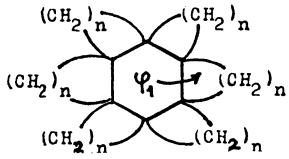
It is well-known that local minima pose a serious problem in molecular mechanics calculations.[20,30] In our case for the molecules **14** and **15** (and for the hypothetical molecules **17**—**19** and **21**) the minimization ends at local minima if one starts from a cyclohexane chair geometry. Only the use of the strongly planarized C_6 rings as input geometry guarantees the achievement of the absolute minimum.

Results and Discussion

The calculated steric energies E_s, heats of formation HOF, and the values of the sum of torsional angles within the C_6 ring in the molecules under investigation α are collected in the Table 1 together with the available experimental results and the calculated data from the literature. The trends exhibited by some torsional angles within the series **9**—**11** and **16**, **17**, and **19** are given in Table 2.

Some remarks should be made on the calculated steric energies. E_s values represent actually energies relative to hypothetical reference system. As such they can be compared on a physically sound basis only for isomers. For obvious reason the values calculated for the *cis*-compounds **5** and **13** are higher than those for the *trans*-molecules. More interesting seems the fact that the closure of the last ring in polycycles **14**—**19** yielded a higher value of the steric energy of [6.4]coronane **17** than the value for **15** while the corresponding values for [6.5]coronane (**16**) and [6.3]coronane (**19**) are lower than the ones for the molecules **14** and **18**, respectively.

Table 2. Calculated and Experimental (in Parentheses) Values of Selected Torsional Angles (in Degrees)

		ϕ_1	ϕ_2
	n=1 (**11**)	−2.9	64.4
	n=2 (**10**)	−30.1	63.8
		(−32.8)[12]	(64.4)[11] a)
	n=3 (**9**)	−47.5	58.0
		(−46.6)	(58.2)[11]
	n=1 (**19**)	0.0	
	n=2 (**17**)	22.6	
	n=3 (**16**)	39.5	

a) This value has not been given in the original Ref. 12 and is incorrectly cited as C5–C9–C8–C7 angle in the Table 5 of the Ref. 11 but the model calculations cited in the former reference prove that this is the largest torsional angle in the C_6 ring.

As was stated above, very few experimental data are known to compare with. Experimental heats of formation values have been reported only for the molecules **9**—**11**[31] and the HOF values for *cis*- and *trans*-**5**, *trans*-**6**, *cis*- and *trans*-**13**, **14**—**19**, and **21** can be considered as an estimation of the values which are very difficult, if possible, to obtain experimentally. The calculated MM2 HOF values for the molecule *cis*-**5** is reasonably close to the corresponding MINDO/3 value calculated in Ref. 32 (see footnote i to the Table 1).

An inspection of the α values collected in the Table 1 seems to indicate that in the cases where the corresponding experimental data have been published there is a reasonable agreement between the calculated and experimental results. The difference is equal to 5° for bicyclo[4.2.0]octane (**10**) and is equal to ca. 20° between the analogous molecules **14** and 13-(3,5-dinitrobenzoyloxy)hexacyclo[12.2.0.0^{1,4}.0^{4,7}.0^{7,10}.0^{10,13}]hexadecane (**22**), and **20** and **21**. It seems that even the last value of 20° is not big since (a) it corresponds to an average error of less than 4° and (b) the molecules in comparison are not identical but rather close analogues.

For the molecules *trans*-**6** and *cis*- and *trans*-**13** the reported experimental data are insufficient to calculate the corresponding α values but the results of the calculations reproduce with a reasonable accuracy the available experimental torsional angles. For example,

†The calculated results of the present paper as well as those of references **11**—**13** for the molecules **9**—**11** reproduce all available experimental data satisfactorily.

††The values of the C_1–C_2 bond length for *cis*- and *trans*-**13** calculated in Ref. 26 are lower than the natural bond lengths which is very unusual.

for *trans*-**6** the central ring has been found to be approximately diplanar with the interplane angle of 163° and the corresponding calculated value is equal to 158°. Similarly, the calculated and experimental values of torsional angles for *cis*- and *trans*-**13** are very close. The angle $\varphi_{4,2,1,7}$ is equal to 16.7° (exp.[17]), 14.9° (calcd MM2, this work), and 14.4° (calcd MM2[26]) for *trans*-**13**; and to 17.9° (exp.[17]), 18.0° (calcd MM2, this work), and 18.8° (calcd MM2[26]) for *cis*-**13**.

The reasonable results obtained for **9**, **10**, **13**, **14**, and **21** and especially those for *trans*-**6** seem to validate the use of molecular mechanics method with the MM2 parameterization to analysis of the flattening in even highly strained cyclohexane rings. The available experimental data and the results of the calculations seem to indicate that fusion of a 3-membered ring or fusion of several 4- and 5-membered rings leads to a similar flattening since the corresponding values are similar for **11** and **15** ($\alpha \cong 135°$) and for *cis*- and *trans*-**13** and for **16** and **18** ($\alpha \cong 200°$). The experimental data for the molecule **15** and **17** are not known at present but synthetic effort by Prof. Fitjer and his group allows to hope that they will be available in the near future. Similarly, the synthesis of *cis*-**5** carried out at present by the Prof. Prinzbach's group should yield another check of the predictive power of the method if the substances will crystallize enabling X-ray analysis to be carried out.

As was stated in Chapter 2, the calculated values for bond angles do not reproduce the experimental ones, but a general trend of enlarging the angles upon ring planarization holds since it is enforced by the conditions of ring closure.

Conclusion

In spite of the inaccuracies in the MM2 parameterization involving cyclopropane ring molecular mechanics calculations seem to reproduce the flattening of a cyclohexane ring upon fusion with small ring(s). The experimental data and the results of the calculations presented in this work seem to indicate that the flattening is more pronounced when smaller and/or more ring(s) are fused to a cyclohexane ring. On the basis of calculations a hypothetical [6.3]coronane is postulated to exhibit a planar C_6 ring. The calculations yielded also an estimation of the HOF values for the molecules *cis*- and *trans*-**13**, **14**—**19**, **21** which are unavailable at present. The value of 4.5 kcal mol^{-1} for the V_3 parameter of the type 22-22-1-22 proposed in the MM2 parameterization is questioned and further refinement of other parameters for highly strained and/or cyclopropane containing molecules is postulated.

Further studies of the molecules with planar cyclohexane rings are in prospects. The synthetic efforts by the Prof. Prinzbach's group in the field of heteroanalogues of *cis*-tris-σ-homobenzenes and those by the Prof. Fitjer's group in the field of coronanes seem especially promising in this respect. If the substances will crystallize they will enable an additional check of the present calculations in the near future.

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