Pergamon

Tetrahedron 58 (2002) 8591–8596

TETRAHEDRON

Conformational properties and intramolecular hydrogen bonding of tetraethyl resorcarene: an ab initio study

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Received 3 May 2002; revised 27 June 2002; accepted 18 July 2002

Abstract—The relative stability of the five extreme conformations of tetraethyl resorcarene was studied by ab initio calculations. The stabilizing effect of intramolecular hydrogen bonding was clearly observed. In addition, the directions of the hydrogen bonds affected the stability, the homodirectional orientation being favoured. The symmetrical C_4 'crown' conformation, having a circular array of hydrogen bonds, was identified as the most stable conformational form of the resorcarene molecule. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Resorcarenes (resorcinarenes) are one-pot synthesisable macrocyclic compounds with several properties that make them of wide interest and use. Among others, these properties include a rigid molecular skeleton, which gives them the capability to act as host molecules. Resorcarenes are mentioned, for example, as host molecules for several types of guest molecules,[1] as monolayer formers on Langmuir–Blodgett films[2] and on gold,[3] as transbilayer tunnels on cells[4] and as building blocks for even larger supramolecular assemblies.[5]

The stereochemistry of resorcarenes is determined by the conformational properties of the resorcinol rings, together with the relative and individual configurational properties of the substituents.[6] The main factor is the orientations of the resorcinol rings, which determine the conformations. The relative orientations of the substituents on the methyl bridges connecting the resorcinol units determine the relative configurational properties. Usually the orientation of one of the substituents is taken as reference. The individual configurational orientations of these substituents are either axial or equatorial.

Resorcarenes are known to exist in five extreme conformational forms. Four of these were introduced by Högberg,[6,7] and the fifth was found later by Abis et al.,[8] both groups using NMR methods. The four Högberg conformations (in parenthesis, synonyms used in some contexts) are crown (cone), boat (pinched cone), chair (partial cone) and saddle (1,3-alternative); the additional fifth conformation is the diamond (1,2-alternative). The nomenclature and the symmetry groups can be found in the literature.[9]

The resorcarene under study is presented in Fig. 1. The trivial name of this molecule is tetraethyl resorcarene.[10] Our reason for choosing this particular resorcarene for modelling was its use in our earlier MS studies.[11] The earlier results suggest that, under the conditions used, tetraethyl resorcarene exists in the crown conformation in both solution and gas phases.

Some molecular modelling has been done earlier on other resorcarenes[12] and on their relative compounds, the calixarenes.[13] The method applied for the resorcarenes was molecular mechanics with MM3 force field. These pioneering studies encouraged us to apply ab initio methods as a tool for clarifying the properties of tetraethyl resorcarene.

2. Computational details

2.1. Optimization calculations

The analysis and the visualization of the results were accomplished using GaussView 2.1, the graphical interface of Gaussian. All ab initio calculations were made with

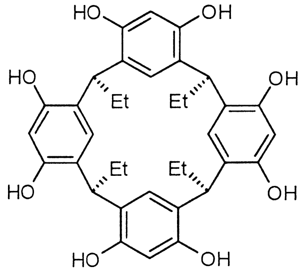

Figure 1. Tetraethyl resorcarene.

Keywords: resorcarenes; ab initio calculations; intramolecular hydrogen bonds; conformation.

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PII: S0040-4020(02)00863-3

Table 1. The calculated energy differences of different structures in kJ mol^{-1}

Structures	Optimisation calculations		Single point energy calculations			
	HF/3-21G	HF/3-21G & 6-31++G(d,p)	HF/6-311++G(d,p)	B3LYP/6-311++G(d,p)	MM/MMFF	Semi-empirical/AM1
Without H-bonds						
Saddle	180.3	170.8	99.5	121.5	109.2	42.5
Chair	167.1	148.2	75.5	98.6	108.5	33.5
Diamond	151.5	125.7	55.1	75.4	104.5	13.9
Boat	145.2	122.3	50.7	71.0	112.9	21.6
With H-bonds						
Pinched crown A	35.6	32.9	21.4	22.5	23.0	11.3
Pinched crown B	33.5	31.3	17.3	24.6	23.2	0.0
Pinched crown C	25.1	22.0	13.7	15.8	14.2	6.9
Pinched crown D	21.3	19.1	12.2	13.1	12.5	8.3
Crown E	0.0	0.0	0.0	0.0	0.0	6.3

Except the semi-empirical, all energies are given relative to the most stable conformer, crown **E**

Gaussian98.[14] The structure optimisation calculations were made by Hartree–Fock (HF) method using (a) the 3-21G basis set and (b) a mixed basis set: 6-3l++G(d,p) for the eight OH-groups and 3-21G for the rest of the molecular skeleton. The larger basis set for the OH-groups was used to clarify the structural and conformational properties due to intramolecular hydrogen bonds. Despite the limitations of the relatively small basis set 3-21G, it is expected to reasonably account for the structures.[15]

The relative stabilities of the conformations were evaluated from the energy differences of the structures. When the presence of intramolecular hydrogen bonds between the resorcinol OH-groups were assumed, the orientations of these bonds were manually adjusted before the calculations.

Except for the chair and diamond conformational forms, all optimization calculations were made on rccc-configurations of the resorcarene ethyl substituents. In the chair conformation the substituent configuration was rctt and in the diamond it was rcct. The reason for choosing these other configurations for the chair and diamond conformations was that optimization calculations made on rccc-configurations of these two conformations bent the molecular skeleton towards the boat conformation (i.e. turned the orientations of the resorcinol rings). Obtaining all five conformations depended on this configurational adjustment.

2.2. Single point energy calculations

The single point energy calculations on the mixed basis set optimised structures were made with HF/6-311++G(d,p). Additional single point energy calculations, carried out to compare the congruence of different methods and levels of theory, were made with B3LYP/6-311++G(d,p), semi-empirical method (AM1) and molecular mechanics (MMFF). The first two of these calculations were made with Gaussian98 and the last two with PC Spartan Pro 1.0.3.[16]

3. Results and discussion

3.1. Conformational forms

The first optimization calculations were made with the intramolecular H-bonding possibilities ignored. In fact, all the conformations could have some intramolecular H-bonding, but in view of the multitude of possibilities, even in a single conformation, all were ignored. In this way the influence of differences in the resorcinol orientations on the stability of the molecular skeleton was emphasized. Four different minimum energy conformations were found. It should be noted that, because the intramolecular H-bonds were ignored, the crown conformational form was not observed at this point.

The results of the optimization calculations without intramolecular H-bonds considered are presented in Table 1. The overall order of the conformations was boat > diamond > chair > saddle. This order is in agreement with results of earlier MM calculations,[12] with one exception: the chair and diamond conformations are transposed. The geometries of the minimum energy conformations are shown in Fig. 2.

The single point energy calculations for the optimised structures produced inconsistent results (Table 1). The results obtained by the HF and B3LYP methods were equivalent, but the MM and semi-empirical methods are strongly dependent on the parametrization and were unable to produce the same trend as observed with HF and B3LYP.

The geometry of the boat conformation seems to be determined by the repulsive forces between the oxygen atoms. The oxygen atoms are located far away from each other and, as a result the molecular skeleton relaxes to the most stable boat conformation possessing minimum energy. This boat has a slightly twisted molecular skeleton, that is, the opposite resorcinols are slightly staggered. Furthermore, the boat conformation does not appear to have any weak intramolecular interactions stabilizing the molecular skeleton.

The relative stability of the diamond conformation was surprisingly similar to that of the boat; the energy difference between the two conformations was minimal. One possible explanation for the stability of the diamond conformation is the close proximity of the ethyl substituents and the upturned resorcinol OH's, which increases the possibility for the formation of weak intramolecular hydrogen bonds.

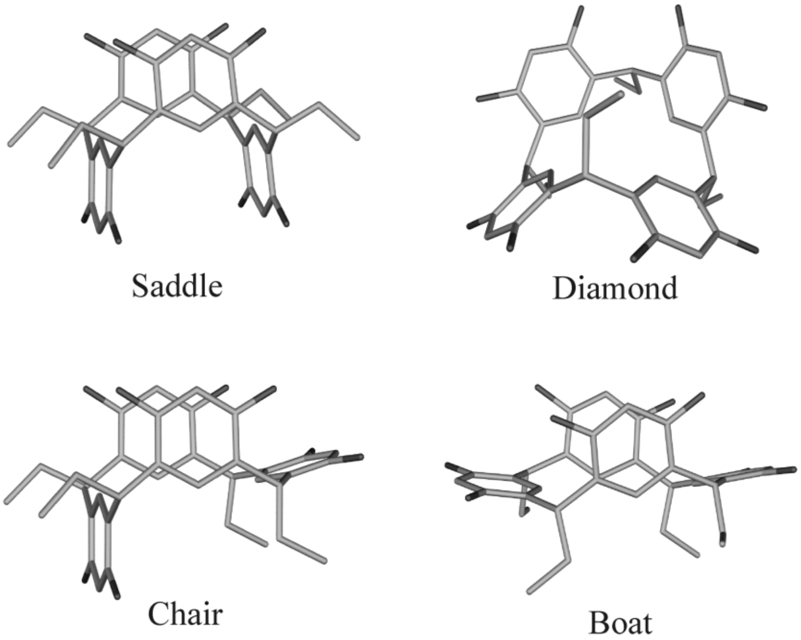

Figure 2. Optimised conformations of the resorcarenes without the intramolecular H-bonds. The hydrogens are omitted for clarity.

The saddle and chair conformations do not have the same kind of possibility to form stabilizing weak interactions. With these conformations the distances between the oxygens may be even longer than in the boat conformation, but evidently the orientations of the resorcinols and ethyl substituents and, furthermore, the possible tensions in the molecular skeleton, are the more important source of high total energy.

3.2. Effect of intramolecular H-bonds

Intramolecular hydrogen bonds can form between the OH-groups of the resorcinol subunits. The total H-bonding network comprises the contributions of the four subsystems between neighbouring resorcinol units. These four OH pairs are, therefore, basically independent of each other. This leads to a total of 81 (3^4) different intramolecular H-bond system combinations where the orientations of the H-bonds differ or the H-bond does not exist.

In the second step of the calculations, the possibility for intramolecular H-bonding was taken into account for the boat conformation, which was found to have the lowest energy. Also, the number of possible intramolecular H-bonds is a maximum with the boat conformation, so it is unlikely that one of the other conformational forms would have a more stable structure with H-bonds included. Only structures with four intramolecular H-bonds were considered in the calculations.

There are theoretically 16 (2^4) different ways in which the boat conformation can form an intramolecular H-bonding system with the maximum number of H-bonds. Five of these are presented (Fig. 3) and discussed here to clarify the stabilizing effect of the intramolecular H-bonding. The forms considered can be described as follows: (in parenthesis, the nomenclature used for the circular hydrogen bonding systems in the water clusters by Saenger[17]) (**A**) the resorcinols forming the 'broadsides' of the boat act as H-bond donors (heterodromic), (**B**) the resorcinols forming the 'stern' and 'bow' act as donors (heterodromic), (**C**) in two opposite semi-circular H-bond arrays, one resorcinol acts as double donor, two resorcinols act as both donors and acceptors, and the fourth resorcinol acts as double acceptor (antidromic), (**D**) in a circular array, one H-bond is reversed (heterodromic), and (**E**) in a complete homodirectional circular H-bond array, all four resorcinols act as both donor and acceptor (homodromic). All these orientations are distinctly different and thus broadly represent the possibilities for intramolecular hydrogen bonding in resorcarenes.

The calculations showed that the intramolecular H-bonding had a marked effect on the stability of the resorcarene skeleton. Relative to the boat conformation without such bonding, it provided a great stabilizing effect, in magnitude up to tens of kJ mol^{-1}. The result argues strongly against the existence of the boat conformation without H-bonds.

3.3. Orientation of intramolecular H-bonds

The orientation of the H-bonding system was an additional noteworthy point. We use the term 'pinched crown' to distinguish the resorcarene structures having intramolecular H-bonds (but not C_4 symmetry) from the boat conformation that lacks intramolecular H-bonds. The crown structure with C_4 symmetry is called '(perfect) crown'.

The intramolecular H-bonding systems in structures **A**, **B**, **C** and **D** do not produce the perfect crown conformation; instead, the molecular skeleton turns more or less to the pinched crown conformation and the equal dimensions disappear. This was most clearly seen with structures **A** and **B**; both favour the C_{2v} pinched crown conformation over the crown. Structures **C** and **D** also have a pinched crown conformation, but the resemblance to the crown conformation is stronger than for **A** and **B**. Only the structure **E** with represents the symmetrical C_4 'perfect' crown.

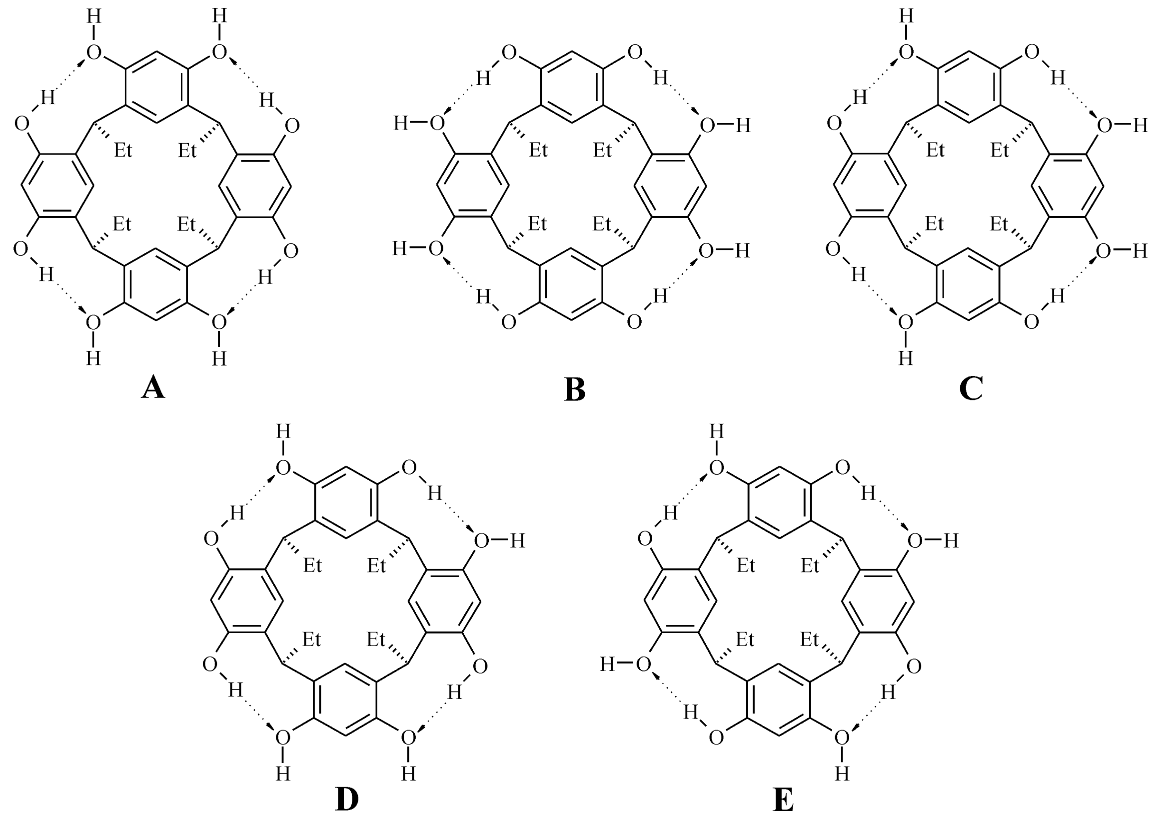

Figure 3. Calculated intramolecular H-bond possibilities.

According to the calculations, the most stable conformational form was **E**, the crown, having a circular intramolecular H-bonding network and C_4 symmetry (Fig. 4). The dimensions of the resorcarene crown are as follows: 'height' is 6.3 Å and 'width' from the upper rim 9.9 Å.

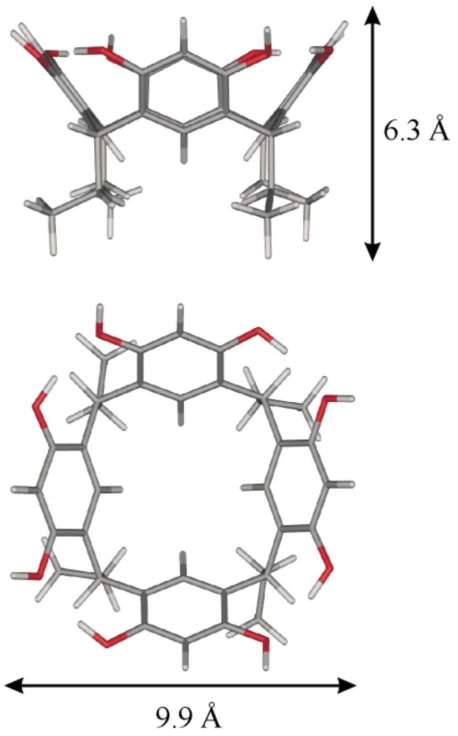

Figure 4. The optimised C_4 crown structure of tetraethyl resorcarene. The dimensions shown are internuclear distances.

The stabilizing effect increases as the H-bonding system becomes more homodirectional and circular. Also, the co-operative action of the same resorcinol as both H-bond acceptor and H-bond donor is favoured. The tendency is as follows. Structures **A** and **B** include two double donor and two double acceptor resorcinols. As a result, half of the H-bonds are in one direction and half in the other, the energy differences between the two structures are minor and the overall energies are higher than for **C**, **D** and **E**. Compared with **A** and **B**, the structures **C** and **D** are more stable; here two resorcinols act as donor–acceptors, one acts as double acceptor and one acts as double donor. Structure **D** is slightly more stable than **C**, obviously because it has three homodirectional H-bonds; **C** includes two semi-circles where the H-bond orientations are opposite. In turn, the crown structure **E** has four donor–acceptor resorcinol units and is by far the most stable structure. The H-bonds are homodirectional, creating a circular H-bonding network and highly symmetrical structure. This co-operative system, in which every resorcinol unit acts as both donor and acceptor, seems to be energetically favourable, creating a stabilizing effect on the molecular skeleton. The effect is so powerful that it dominates even though the molecular skeleton is less relaxed than in the boat-like pinched crown conformation (which might be assumed to be the more stable structure). This relaxation tendency was also tested with a separate optimization calculation; when the intramolecular H-bonds of the C_4 crown were removed, the molecular skeleton turned to the C_{2v} boat conformation. The same observation has been made earlier: complete acylation of the OH-groups transformed the skeleton from crown to boat, as the circle of hydrogen bonds was broken.[18]

The calculated energies between the intramolecular H-bonded resorcarenes were in favour of the circular system. Another noteworthy point was that a change in direction of a single H-bond caused a drastic decrease in the overall stability. These results are in accordance with the results obtained to the water clusters: both experiments and calculations yielded cyclic homodromic structure for the trimer and the tetramer at the energy minimum.[19] As for the conformational forms, the results achieved with different methods of calculation were more or less the same, except for the results of the semi-empirical method, which were clearly divergent.

One additional point is relevant to the intramolecular H-bonding system of resorcarenes. This is the so called ‘flip-flop’ H-bonding system, where the orientations of the H-bonds change in every OH-pair. This kind of movement is claimed to be energetically favourable relative to static H-bonds.[20] The result of our earlier mass spectrometric study on hydrogen/deuterium (H/D) exchange reactions were consistent with the presence of the flip-flop system in tetraethyl resorcarene.[21] The flip-flop system has also been suggested for calixarenes on the basis of NMR measurements.[22] Our calculations did not preclude the existence of the flip-flop phenomena, and further calculations for investigating such a H-bonding system in resorcarenes are in progress.

4. Conclusions

The conformational forms and the influence of the intramolecular H-bonding of tetraethyl resorcarene were calculated by ab initio methods. Without inclusion of the intramolecular H-bonds, the boat conformation is found to be the most stable conformational form. When the intramolecular H-bonds in the boat conformation are taken into account, the conformational stability increases markedly, and also the relative positions of the resorcinol units change; for this reason the hydrogen bonded boat conformations are more accurately called pinched crown conformations. Additional stabilization is provided by the directions of the H-bonds: the stability of the molecular skeleton increases with increased homodirectionality of the H-bonds.

When stabilizing intramolecular H-bonds are added, the crown is identified as the most stable conformation. The crown has a circular homodirectional intramolecular hydrogen bonding system and C_4 symmetry. In this conformation, every resorcinol subunit acts simultaneously as H-bond donor and H-bond acceptor. Evidently it is the co-operative H-bonding network that makes this the most stable conformational form although there is more tension in the molecular skeleton than in the boat or pinched crown conformations.

All energy calculations except the semi-empirical yielded more or less similar results. The results obtained for this particular resorcarene are expected to reflect the conformational properties of all correspondingly substituted resorcarenes. Further optimization calculations with higher levels of theory are planned, but they are expected to confirm the general picture presented here.

Acknowledgments

Funding by the Academy of Finland, Grant 68194, is gratefully acknowledged.

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