

Structure and conformational equilibrium of new thiacalix[4]arene derivatives

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Abstract

Density functional theory was used to study the structure and conformational equilibrium of tetraaminothiacalix[4]arene (**1**) and tetramercaptothiacalix[4]arene (**2**), which are expected to open a new area of host–guest chemistry. All the calculations predict the *cone* as the most stable conformer for both compounds, which is in good agreement with an earlier theoretical study on the parent thiacalix[4]arene. It is shown that different substituents at the lower rim do not affect the stability ordering. The intramolecular bonding between hydrogen atoms and sulfur bridges seems to be a dominant factor in stabilizing all the conformers rather than hydrogen bonds between the groups of the lower rim.

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1. Introduction

Calixarenes belong to an interesting class of macrocyclic molecules consisting of polyphenolic units linked by methylene bridges at *ortho* positions with respect to the hydroxyl groups, which reveal a basket-shaped structure [1]. The growing interest on calixarenes is certainly due to their versatility in terms of complexing abilities, conformational flexibility and reactivity, and their applications have been used in a wide diversity of areas as catalysis, host–guest chemistry, separation chemistry, selective ion transport and sensors [1–3]. In addition, calixarenes have provided versatile basic platforms for excellent host compounds in supramolecular chemistry via chemical modifications. First, complete or partial functionalizations of calixarenes have been performed at their lower (phenolic OH groups) and/or upper rims (the *p*-position) [3–5]. Recently, the replacement of the bridging CH₂ groups by heteroatoms has been achieved [6–11], which is the case of the well known thiacalixarene, where the CH₂ bridges are replaced by S atoms. The increasing number of coordi-

nation sites leads to significant changes of its chemistry and a large diversity in its host–guest properties [12–18], especially the inclusion complexes with transition metal ions [14–18].

Recently, density functional theory (DFT) methodology has been applied successfully in the theoretical investigation of calixarenes [19–21]. In this work, we also report DFT calculations for the structure and conformational equilibrium of new thiacalix[4]arene derivatives namely tetraaminothiacalix[4]arene (**1**) and tetramercaptothiacalix[4]arene (**2**), in which the four OH groups at the lower rim of thiacalix[4]arene are substituted by NH₂ and SH groups, respectively. The main goal of this study is to understand how the presence of different substituents at the lower rim of thiacalix[4]arene modifies its conformational flexibilities and binding abilities relative to a previous study performed at DFT level on parent thiacalix[4]arene [22].

2. Computational methods

The geometries of the four main conformers of compounds **1** and **2** were optimized completely without any constraints at the restricted Hartree–Fock (RHF) level with the 6-31G(d) basis set. These geometries were

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used afterwards as input for final geometry optimizations at DFT level using B3LYP method as a combination of the Becke's three parameter hybrid exchange functional [23] and the Lee, Yang and Parr correlation functional [24] with the 6-31G(d,p) basis set. The energies for these optimized structures were also obtained by additional single point calculations with the B3LYP and B3PW91 functionals (the latter includes a correlation functional proposed by Perdew and Wang in 1991 [25–27]), with the 6-311G(d,p) basis set. All the electronic calculations were carried out with the GAUSSIAN 98 program package [28].

3. Results and discussion

3.1. Structure, hydrogen bonding and charge distribution of thiacalix[4]arene derivatives

The DFT optimized structures of the four conformers named *cone*, *partial cone* (*paco*), *1,2-alternate* (*1,2-alt*) and *1,3-alternate* (*1,3-alt*) of the compounds **1** and **2** are presented in Fig. 1. Unfortunately, neither of these compounds has been obtained yet, by experimental synthesis but similar compounds were synthesized namely the tetraamino-*p-tert*-butylthiacalix[4]arene [29] and the tetramercapo-*p-tert*-butylthiacalix[4]arene [30]. Some relevant geometrical parameters of *cone* conformers of the compounds **1** and **2** and of parent thiacalix[4]arene [22] obtained at B3LYP/6-31G(d,p) level are presented in Table 1 and Fig. 2. We observe that most bond distances and bond angles are not sensitive to substituent groups at the lower rim. The X–X distance depends on the atomic size and steric hindrance. The results show that the *cone* conformer of both compounds presents C_2 -like symmetry rather than the C_4 symmetry obtained for the thiacalix[4]arene [22], as the X_1 – X_3 and X_2 – X_4 distances are not identical anymore, and the angles ϕ (see Table 1) between two opposite benzene rings are also not consistent.

As expected, structures show important hydrogen bonds that contribute greatly to the stabilization of the conformations. The most favorable arrangement of hydrogen bonds for both *cone* and *paco* conformers of compound **1** shows two amino groups playing as donors and the others as acceptors. It differs from the parent thiacalix[4]arene, where each amino group acts simultaneously as a donor and as an acceptor. It is interesting to note that hydrogen bond distances (NH–N) and bond valence angles (N–H–N) are 2.28 Å and 167°, respectively, while in thiacalix[4]arene the former parameter was predicted to be 1.82 Å [22].

Partial charges for *cone* conformer of both compounds are reported in Table 2. The charges were calculated by using the Merz–Kollman–Singh (MK) scheme [31,32] at B3LYP/6-31G(d,p) level, which is a fitting of point

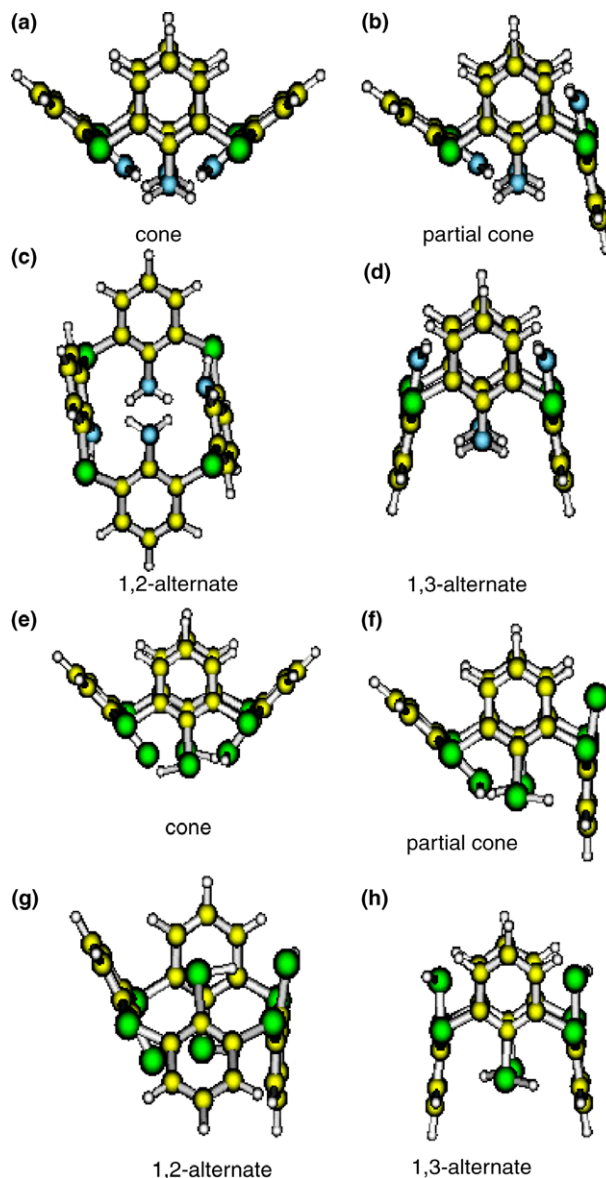


Fig. 1. Optimized geometry of the four main conformers of (a)–(d) tetraaminothiacalix[4]arene (**1**) and (e)–(h) of tetramercaptothiacalix[4]arene (**2**) obtained at B3LYP/6-31G(d,p) level.

charges, selected on a set of concentric spheres around each atom, to the calculated electrostatic potential. For simplicity, and owing to the C_2 -like symmetry of the systems, we present only data for two benzene rings and the sulfur bridged unit. The high negative charges of donor atoms are predicted to follow the order: $NH_2 > OH > SH$. The bridging sulfur in both compounds exhibit more negative charge when compared with parent thiacalix[4]arene. It may be suggested that the new sulfur bridged compounds exhibit a dominant character for metal ion in that region. This is in good agreement with experimental information [33,34], which showed that two tetraamino-*p-tert*-butylthiacalix[4]arene can bind to two Pd(II) ions with a *trans*-square planar coordination

Table 1
Structural parameters for *cone* conformer of thiacalix[4]arene derivatives at B3LYP/6-31G(d,p) level

	Tetraaminothiacalix[4]arene	Tetramercaptothiacalix[4]arene	Thiacalix[4]arene ^a
<i>Bond distance^b (Å)</i>			
S ₁ '–C ₁	1.80	1.80	1.80
C ₁ –C ₂	1.42	1.42	1.41
C ₂ –X ₁	1.36	1.77	1.36
C ₂ –C ₃	1.42	1.42	1.41
C ₃ –S ₂ '	1.80	1.80	1.80
S ₂ '–C ₄	1.81	1.81	1.80
C ₄ –C ₅	1.41	1.41	1.41
C ₅ –X ₂	1.40	1.78	1.36
C ₅ –C ₆	1.41	1.42	1.41
C ₆ –S ₃ '	1.81	1.81	1.80
S ₃ '–C ₇	1.80	1.80	1.80
C ₇ –C ₈	1.42	1.42	1.41
C ₈ –X ₃	1.36	1.77	1.36
C ₈ –C ₉	1.42	1.42	1.41
C ₉ –S ₄ '	1.80	1.80	1.80
S ₄ '–C ₁₀	1.81	1.81	1.80
C ₁₀ –C ₁₁	1.41	1.41	1.41
C ₁₁ –X ₄	1.40	1.78	1.36
C ₁₁ –C ₁₂	1.41	1.42	1.41
C ₁₂ –S ₁ '	1.81	1.81	1.80
X ₁ –X ₂	3.27	3.94	2.74
X ₂ –X ₃	3.27	3.82	2.74
X ₃ –X ₄	3.27	3.94	2.74
X ₄ –X ₁	3.27	3.82	2.74
X ₁ –X ₃	3.56	3.71	3.87
X ₂ –X ₄	5.41	6.81	3.87
<i>Angle (°)</i>			
C ₁₂ –S ₁ '–C ₁	102.8	100.2	104.3
S ₁ '–C ₁ –C ₂	121.5	121.3	120.7
C ₁ –C ₂ –X ₁	121.5	118.0	122.2
C ₂ –C ₃ –S ₂ '	121.5	122.5	120.7
C ₃ –S ₂ '–C ₄	102.8	100.0	104.3
S ₂ '–C ₄ –C ₅	119.8	120.9	120.7
C ₄ –C ₅ –X ₂	120.6	118.4	122.2
C ₅ –C ₆ –S ₃ '	119.8	122.1	120.7
C ₆ –S ₃ '–C ₇	102.8	100.2	104.3
S ₃ '–C ₇ –C ₈	121.5	121.3	120.7
C ₇ –C ₈ –X ₃	121.5	118.0	122.2
C ₈ –C ₉ –S ₄ '	121.5	122.5	120.7
C ₉ –S ₄ '–C ₁₀	102.8	100.0	104.3
S ₄ '–C ₁₀ –C ₁₁	119.8	120.9	120.7
C ₁₀ –C ₁₁ –X ₄	120.6	118.4	122.2
C ₁₁ –C ₁₂ –S ₁ '	119.8	122.1	120.7
ϕ^c (°)	109.1;7.2	95.5;26.4	77.2;77.4

Atom numbering according to Fig. 2.

^a From [22].

^b X is denoted to the atom N, S and O for tetraaminothiacalix[4]arene, tetramercaptothiacalix[4]arene and thiacalix[4]arene, respectively.

^c ϕ is the angle between two opposite benzene rings.

geometry via two sets of sulfur and nitrogen atoms. Furthermore, Au(III) and Pd(II) ions were extracted from acidic solutions containing 41 different metal ions by forming complexes with this ligand [33]. Interestingly, the distribution of atomic charges of carbon atoms in the benzene ring are different in the three compounds. This may lead to different strength of complexation of thiacalix[4]arene derivatives through cation– π electron interactions.

3.2. Energetics and conformational equilibrium of thiacalix[4]arene derivatives

The conformational equilibrium data obtained at DFT level for both compounds are reported in Table 3 where the energy of *cone* conformer is taken as reference. The energetic ordering for both compounds was predicted to be: *cone* < *paco* < *1,3-alt* < *1,2-alt*, the most stable conformer being the *cone*. The additional NH–S'

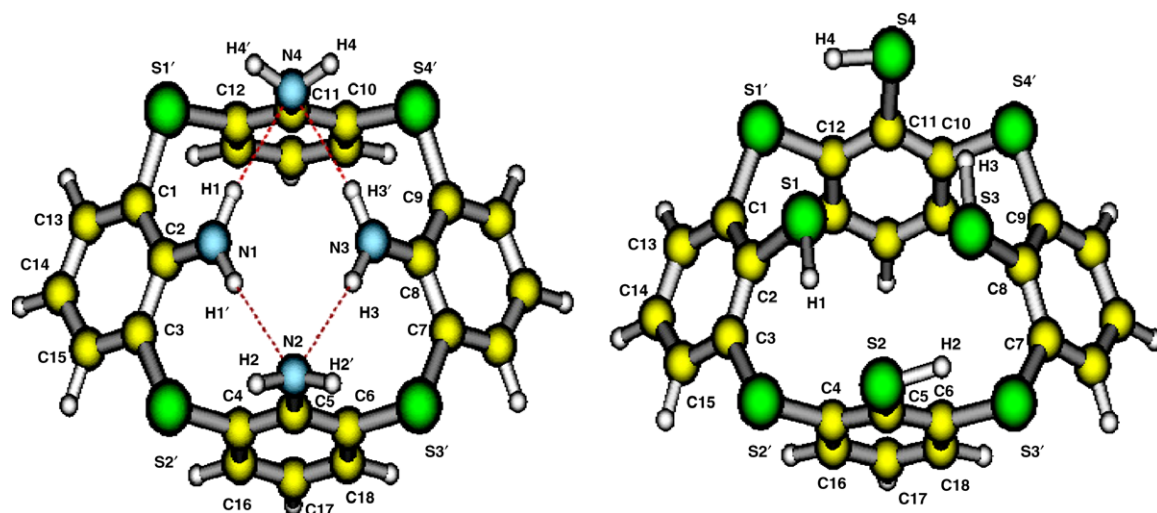


Fig. 2. Optimized *cone* structures for tetraaminothiacalix[4]arene (**1**) and tetramercaptothiacalix[4]arene (**2**) obtained at B3LYP/6-31G(d,p) level.

Table 2

MK atomic charges (in e) for the *cone* conformer of thiacalix[4]arene derivatives at B3LYP/6-31G(d,p) level

Atoms ^a	Tetraaminothiacalix[4]arene	Tetramercaptothiacalix[4]arene	Thiacalix[4]arene ^b
C1	0.13	0.41	-0.12
C2	0.10	-0.33	0.39
C3	0.13	0.36	-0.16
X1	-0.55	-0.19	-0.42
H1	0.23	0.19	0.30
H1'	0.23		
S1'	-0.24	-0.27	-0.13
C13	-0.09	-0.21	0.04
C14	-0.30	-0.15	-0.31
C15	-0.09	-0.20	0.04
C4	-0.01	0.25	
C5	0.31	-0.03	
C6	0.01	0.17	
X2	-0.51	-0.20	
H2	0.26	0.21	
H2'	0.26		
S2'	-0.24	-0.24	
C16	-0.18	-0.33	
C17	-0.09	0.03	
C18	-0.19	-0.27	

Atom numbering according to Fig. 2.

^aX is denoted to the atom N, S and O for tetraaminothiacalix[4]arene, tetramercaptothiacalix[4]arene and thiacalix[4]arene, respectively.

^bFrom [22].

bonding between amino groups and sulfur bridges is also observed in compound **1**. The NH–S' bond distance and the N–H–S' bond angle of *cone* conformer at B3LYP/6-31G(d,p) level are approximately 2.58 Å and 106.5°, respectively. The optimized *cone* and *paco* conformers of the compound **1** reveal an interesting array of hydrogen bonds between the amino groups, and between the N–H hydrogens and the sulfur bridges, which seems to contribute greatly to stabilize these conformations. On the other hand, the *1,3-alt* conformers is stabilized only by NH–S' bondings. Even though the steric hindrance and weaker acceptor character of thiol groups (–SH) in compound **2** seems to be less effective as

intramolecular hydrogen bond, the orientation of the –SH hydrogens towards sulfur bridges may contribute to stabilize all the conformations much more than the hydrogen bond between –SH groups. This is supported by the shorter SH–S' bond distance (2.50 Å) when compared with the SH–S hydrogen bond distance (2.73 Å) of *cone* conformer at B3LYP/6-31G(d,p) level (see Fig. 2).

The same ordering stability was also obtained in a previous theoretical study of the thiacalix[4]arene [22]. It seems that the nature of substituent groups at the lower rim does not affect the conformational equilibrium. However, we found a reduction of ΔE in both compounds for all conformers, specially for compound **1**

Table 3

Relative energy difference (ΔE , in kcal mol⁻¹) of the main conformers of thiacalix[4]arene derivatives at different DFT levels

	<i>cone</i>	<i>Partial cone</i>	<i>1,2-alternate</i>	<i>1,3-alternate</i>
Tetraaminothiacalix[4]arene: compound 1				
B3LYP/6-31G(d,p) ^a	0.00	1.41	6.83	4.11
B3LYP/6-311G(d,p) ^b	0.00	1.37	6.70	4.38
B3PW91/6-311G(d,p) ^b	0.00	0.89	6.48	2.97
Tetramercaptothiacalix[4]arene: compound 2				
B3LYP/6-31G(d,p) ^a	0.00	1.81	4.97	2.04
B3LYP/6-311G(d,p) ^b	0.00	2.16	5.15	2.10
B3PW91/6-311G(d,p) ^b	0.00	2.68	5.85	2.75
Thiacalix[4]arene				
B3LYP/6-31G(d,p) ^c	0.00	10.1	16.5	13.8
B3LYP/6-311G(d,p) ^c	0.00	9.1	15.6	12.3

The energy of the most stable *cone* conformer was taken as reference.

^a Geometry was optimized at this level of the theory.

^b Geometry was optimized at B3LYP/6-31G(d,p).

^c From [22].

when compared with thiacalix[4]arene at same level of DFT calculation. It may be suggested that the weaker intramolecular hydrogen bonds of both compounds reduce the relative stabilization of the conformers, as the breaking of a hydrogen bond when the molecule changes to a less stable conformer is not so energetically unfavourable. It is interesting to realize from Table 3 that the PW91 correlation functional with Becke's three parameters hybrid exchange functional decreases ΔE for all the conformers of compound **1**, when compared with LYP correlation functional. However, in compound **2**, we found an opposite behavior.

Interestingly, it was concluded from experiment that tetraamino-*p-tert*-butylthiacalix[4]arene adopted a typical pinched-cone conformation upon complexation with Pd(II) ion [34], which contrasted with the geometry of the uncomplexed *1,3-alt* conformer obtained in the solid state [29]. All our calculations indicate that there is a small energy difference between these conformers of ca. 3.0–4.5 kcal mol⁻¹ in compound **1**. It may be advanced that interconversion between both conformers can occur. Additional single point calculations at B3LYP/6-311G(d,p) level show that the relative stability ordering of *paco* and *1,3-alt* of compound **2** is reversed when compared with B3LYP/6-31G(d,p) results. However, all the calculations indicate that there is a small energy difference between these conformers of about 0.1–0.2 kcal mol⁻¹. This also suggests that interconversion between both conformers can also occur easily because this molecular system is very flexible and its potential energy surface presents many local minima.

4. Conclusion

The four main conformers of the new tetraaminothiacalix[4]arene (**1**) and tetramercaptothiacalix[4]arene (**2**) were studied by a DFT approach. Our results predict

the stability ordering: *1,2-alternate* < *1,3-alternate* < *partial cone* < *cone*, which is in a good agreement with previous theoretical study on parent thiacalix[4]arene. It is interesting to realize that different substituents at the lower rim do not modify the stability ordering. However, the small difference in the relative energies of the conformers suggests an easy interconversion. The intramolecular bonding between hydrogen atoms and sulfur bridges seems to be a dominant stabilization factor rather than hydrogen bonds between the groups at the lower rim. In these two new compounds the increasing number of coordination sites from substituent groups and sulfur bridges opens a new and diverse range of host–guest properties, especially the specific inclusion complexes with transition metal ions.

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