Computational Insight into Conformational Rearrangement and Intramolecular-H Bond Analysis of Some Calix[4]Arenes Including Acryloyl Moiety

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ABSTRACT

The conformational analyses of Calix[4]arenes reveals four different stable structures (conformations); Cone, Partial Cone, 1,2-Alternate and 1,3-Alternate after employing a density functional theory (DFT) computational analysis. Intramolecular Hydrogen Bonds (IHBs) existing Calixarene core cause Cone conformation, supporting to be the best stable state in 1, 2 and 3 compounds. In addition, one needs Natural Bond Orbital (NBO) analyses of current compounds in order to understand nature of these IHBs. Specifically, it has been shown using NBO that the LP $^*\rightarrow\sigma$ interactions for O$\cdots$O$^-$H IHBs and the delocalization LP $\rightarrow \pi^*$ for O$^-$C=O are the major contributions to energy stabilization. Of all conformers of compound 4, Partial Cone has the lowest energy, which can be attributed to devoid of intramolecular hydrogen bond due to the absence of free phenolic groups.

Keywords:
Calix[4]arene; Acryloyl moiety; Conformational equilibrium; DFT; NBO.

INTRODUCTION

Calixarenes are macrocyclic compounds, which are utilized in important fields like pharmacy, engineering and medicine. They are applied as sensors in various areas of human activities, in medical applications and environmental protection (1, 2). Moreover, they are used in catalysis as well as in molecular recognition. Their cage-like structures play important role in host-guest mechanism in supramolecular chemistry (1, 2). In addition, the functionalization of Calixarenes by means of substituting methylene bridges with heteroatoms is quite important in order to discover new compounds (1, 2). Calixarenes attract much attention due to the rich conformational possibilities which come in four varieties: Cone, Partial Cone, 1,2-Alternate and 1,3-Alternate (3-6).

The four forms of Calixarenes are mainly due to the free rotation of methylene groups. The determination of stable conformations could not always be achieved correctly by spectroscopic techniques such as IR and NMR. On the other hand, the current state of theory on predicting Calixerarene derivatives remains inconclusive or insufficient (7) hence there is still need for extensive theoretical work. Moreover, in literature, it has been highlighted that the determination of the conformational stability from experimental results of Calixarenes

derivatives could be complicated (8), thus, justifies the importance of more theoretical studies.

The main goal in this study is to scrutinize the conformational stability and the effect of intramolecular hydrogen bonds on this equilibrium of some Calix[4]arene derivatives including acryloyl moiety using first principles calculations based on Density Functional Theory (DFT). For this purpose, the most stable states of the compounds were investigated in detail by taking into account all cases including Cone **(C)**, Partial Cone **(PC)**, 1,2-Alternate **(1,2-A)** and 1,3-Alternate **(1,3-A)**. In the next section, we will explain material and methods and computational method used in geometry optimizations of the current molecules. Later, we will discuss our results and summarize our study in conclusion part.

MATERIAL AND METHODS

In Fig. 1, the structures that are previously reported experimental synthesis and spectral characterization are depicted. These reported experimental results have been used as the starting point for the following computational study (9, 10). An X-Ray crystallography of the compound **2** is also available (10) and is used as initial configuration in following DFT calcu-
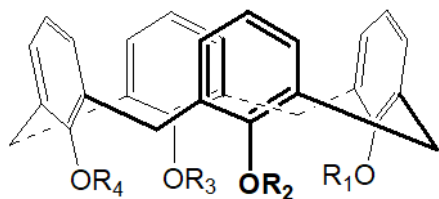
1 R₁= COCH=CH₂, R₂R₃R₄= H

2 R₁, R₄ = COCH=CH₂, R₂,R₃= H

3 R₁, R₂, R₃= COCH=CH₂, R₄= H

4 R₁, R₂, R₃, R₄= COCH=CH₂

Figure 1. The structures of Calix[4]arene derivatives including acryloyl moiety.

lations. These molecules are some Calix[4]arenes derivatives containing acryloyl moiety, in which they consist of p-substituted phenolic units linked by methylene bridges in the ortho position relative to the OH groups (1, 9). These relevant compounds have two usual positions, lower rim (hydroxyl groups) and upper rim (para position as to the hydroxyl groups), as shown in Fig 1.

Computational Method

The conformational equilibrium of Calix[4]arenes derivatives containing acryloyl moiety was examined by using DFT method with B3LYP functional at 6-31G(d,p) level. All possible conformers, i.e. **C**, **PC**, **1,2-A** and **1,3-A**

were relaxed at optimization stage. While all geometries were drawn using Gauss View 5.0 program (11), X-Ray starting geometry of compound **2** was created by taking crystal information file (cif) containing X-Ray coordinates from literature (10). Babel program (12) was used in order to transfer these coordinates into the Z-matrix format. Gaussian 09 program (13) was used in order to relax of all molecules. The intramolecular hydrogen bonding energies were calculated using NBO 3.1 program (14) as implemented in Gaussian 09 program. The molecular electrostatic potentials (MEPs) were drawn in order to see intramolecular H-bond sites. The HOMOs and the LUMOs were illustrated and the global reactivity parameters were computed.

RESULT AND DISCUSSION

Conformational Analysis of the Compounds

In molecules having hydroxyl group, Cone conformation was found to be the most stable state (molecule **1**, **2** and **3** contain three, two and one hydroxyl group, respectively, as shown Fig. 2.) Hydroxyl groups led to conformational rigid structures, i.e. fixed conformations such as Cone, by means of strong O⁻H···O IHBs in the molecules. DFT analysis indicated the molecule 3 exists in Cone. However, Cone has only 0.11 kcal/mol lower energy than Partial Cone as shown in Table 1. As a result, it is apparent that this molecule adopts a Cone conformation since it contains at least one free phenolic group. A study on Calix[4]arene molecule which has one free hydroxyl group revealed that this molecule could exist in both confor-
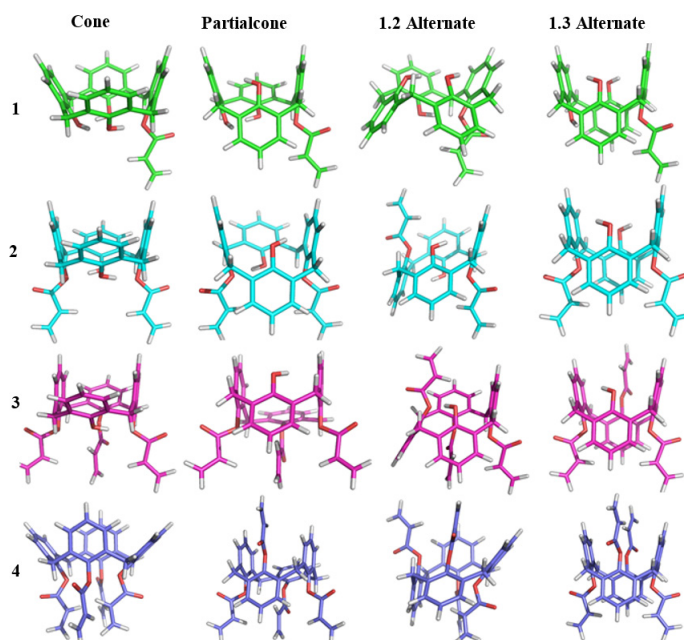

Figure 2. All possible conformers of Calix[4]arene derivatives including acryloyl moiety.

Table 1. Optimization energies of conformers of compounds **1**, **2**, **3** and **4**.

Comp.	Conformer	E (hartree)	ΔE kcal/mol
	Cone	-1573.1375732	0.0
1	Partial cone	-1573.1275896	6.26
	1,2-Alternate	-1573.1216164	10.01
	1,3-Alternate	-1573.1214976	10.09
	Cone	-1763.8625073	0.0
	Experimental[a]	-1763.8613754	0.71
2	Partial cone	-1763.8601678	1.47
	1,3-Alternate	-1763.8572642	3.29
	1,2-Alternate	-1763.8536385	5.57
	Cone	-1954.5940627	0.0
3	Partial cone	-1954.593894	0.11
	1,3-Alternate	-1954.5922281	1.15
	1,2-Alternate	-1954.5911824	1.81
	Partial cone	-2145.3287422	0.0
4	1,3-Alternate	-2145.3283142	0.27
	1,2-Alternate	-2145.3263679	1.49
	Cone	-2145.3154581	8.34

[a] Experimental starting geometry was taken from X-ray coordinates (10).

Figure 3. The comparison of optimized model geometry (blue) with optimized experimental geometry (pink) of compound **2**, where O⁻H···O distances are 1.893 Å and 1.878 Å, respectively.

mations, where one of these conformations is Partial Cone in according to NMR and second one is Cone in according to both IR and DFT. It is also reported that there is a swift exchange between Cone and Partial Cone conformations (15). Moreover, our conformational analysis of compound 4 revealed that the Partial Cone is the most stable state. In the literature, it is emphasized that Calix[4]arenes prefer the Partial Cone or 1,3-Alternate conformers since they are lacking of free phenolic groups (16). In order to find exact conformation of compound 4, we employed a DFT method which predicts the exact conformation as Partial Cone.

When the energy of the model geometry of compound **2** is compared with that of experimental geometry, it is seen a difference of 0.71 kcal/mol, as shown in Table 1. The reason of this difference can be attributed to hook-shaped direction of carbonyl groups of the acryloyl moiety in X-ray geometry (Fig. 3). This is due to steric effect of solvent toluene, as understood from experimental study (10). The experimental realization also confirms that compound **2** prefers Cone conformation due to the intramolecular

Table 2. Hydrogen-bond geometries (Å, °) of compound 1, 2 and 3.

Molecule		D—H···A	D—H	H···A	D···A	D—H···A
		O1—H1···O2	0.980	1.741	2.687	161.2
1	Model optimization	O2—H2···O3	0.984	1.729	2.686	163.2
		O3—H3···O4	0.977	1.800	2.773	173.3
	Experimental[a]	O1—H1···O2	0.91 (11)	2.00 (11)	2.897 (3)	170 (9)
		O3—H3···O4	0.79 (8)	2.11 (8)	2.855 (4)	157 (8)
2	Exp_optimization	O1—H1···O2	0.970	1.878	2.843	173.5
		O3—H3···O4	0.970	1.877	2.843	173.5
	Model_optimization	O1—H1···O2	0.970	1.893	2.852	169.4
		O3—H3···O4	0.970	1.893	2.852	169.4
3	Model _ptimization	O1 — H1···O2	0.968	2.024	2.975	166.6
4		There is no intramolecular hydrogen bonding				

[a] These results were taken from literature (10).

Table 3. Stabilization energies (kcal/mol) of selected NBO donor-acceptor pairs in NBO basis at B3LYP/6-31g(d,p)//B3LYP/6-31g(d,p) level for **1**, **2** and **3** compounds.

Comp.	Φ_i	Φ_j	$E_{ij}^{(2)a}$ (kcal/mol)	$\varepsilon_j - \varepsilon_i^b$ (a.u.)	F_{ij}^c (a.u.)
	LP_1O_9	$\sigma^* O_{55}^- H_{58}$	9.25	1.05	0.088
	LP_2O_9	$\sigma^* O_{55}^- H_{58}$	12.92	0.79	0.092
	LP_1O_{34}	$\sigma^* O_9^- H_{59}$	16.90	1.02	0.118
1	LP_2O_{34}	$\sigma^* O_9^- H_{59}$	7.38	0.78	0.069
	LP_1O_{47}	$\sigma^* O_{34}^- H_{57}$	14.46	1.03	0.110
	LP_2O_{47}	$\sigma^* O_{34}^- H_{57}$	1.26	0.80	0.029
	LP_2O_{47}	$\pi^* C_{48}^- O_{49}$	39.01	0.34	0.105
	LP_1O_9	$\sigma^* O_{62}^- H_{66}$	9.47	1.05	0.090
	LP_2O_9	$\sigma^* O_{62}^- H_{66}$	0.73	0.82	0.023
2	LP_1O_{54}	$\sigma^* O_{41}^- H_{64}$	9.48	1.05	0.090
	LP_2O_{54}	$\sigma^* O_{41}^- H_{64}$	0.73	0.82	0.023
	LP_2O_9	$\pi^* C_{10}^- O_{11}$	40.44	0.34	0.106
	LP_2O_{54}	$\pi^* C_{55}^- O_{56}$	40.44	0.34	0.106
	LP_1O_{54}	$\sigma^* O_{41}^- H_{71}$	4.51	1.05	0.062
	LP_2O_{54}	$\sigma^* O_{41}^- H_{71}$	1.90	0.81	0.037
3	LP_2O_9	$\pi^* C_{10}^- O_{11}$	42.65	0.34	0.108
	LP_2O_{54}	$\pi^* C_{55}^- O_{56}$	38.58	0.34	0.104
	LP_2O_{62}	$\pi^* C_{63}^- O_{64}$	43.07	0.33	0.109

[a] $E^{(2)}$: stabilization energy, [b] Energy difference of i (donor) and j (acceptor) NBO orbitals, [c] Fij: the Fock matrix element.

hydrogen bond between hydroxyl and acryloyl groups (9). This result is in accordance with our theoretical results in terms of both conformational research and intramolecular hydrogen bond analysis. The optimization results regarding to intramolecular hydrogen bonding of X-Ray geometry of compound **2** were listed in Table 2 as Exp optimization line.

The intramolecular hydrogen bond of 1 is stronger than that of both 2 and 3 (Table 2). These results are in line with NBO analysis results, as shown in Table 3. The short O ···O distance means the presence of robust intramolecular H-bonds. Also, the molecular electrostatic potential graphs represent the intramolecular H-bond sites as the electron-rich region in acceptor oxygens of both acryloyl moiety and the hydroxyl groups, while presenting the phenyl rings as the neutral region.

As shown in Fig. 4, HOMOs are partially distributed on Calix[4]arene core with a hydroxyl group, while LUMOs are located partially on acryloyl groups of all molecules. According to Column ΔE from top to bottom in Table 4, HOMO-LUMO energy gaps are gradually increasing, which indicate the molecules become more rigid as it can also be understood from η value.

CONCLUSION

An exhausting search of conformal configurations of Calix[4]arene derivatives including acryloyl moiety is the main promise of this work. Exclusively, compound 4 aside from others, the exact conformation could not be determined exactly by experimental methods (NMR or IR) since there is no -OH group being capable of intra-

Karayel/ Hittite J Sci Eng, 2019, 6 (3) 223–228

Table 4. HOMO-LUMO energies and calculated global reactivity parameters of Calix[4]arenes.

Comp.	E_{homo}(eV)	E_{lumo}(eV)	ΔE(eV)	χ(eV)	μ(eV)	η(eV)	σ(eV)$^{-1}$	ω(eV)
1(Cone)	-5.49969	-1.66969	3.8300	3.5847	-3.5847	1.9150	0.2611	3.3551
2(Cone)	-5.60010	-1.62071	3.9794	3.6104	-3.6104	1.9897	0.2513	3.2756
3(Cone)	-5.74541	-1.68711	4.0583	3.7163	-3.7163	2.0291	0.2464	3.4032
4(Partial Cone)	-6.33944	-1.48057	4.8589	3.9100	-3.9100	2.4294	0.2058	3.1465

ΔE: $E_{LUMO} - E_{HOMO}$, χ:Electronegativity, μ:Chemical potential, η:Chemical hardness, σ:Global softness, ω:Electrophilicity index

HOMO LUMO MEP

ΔE=3.83 eV
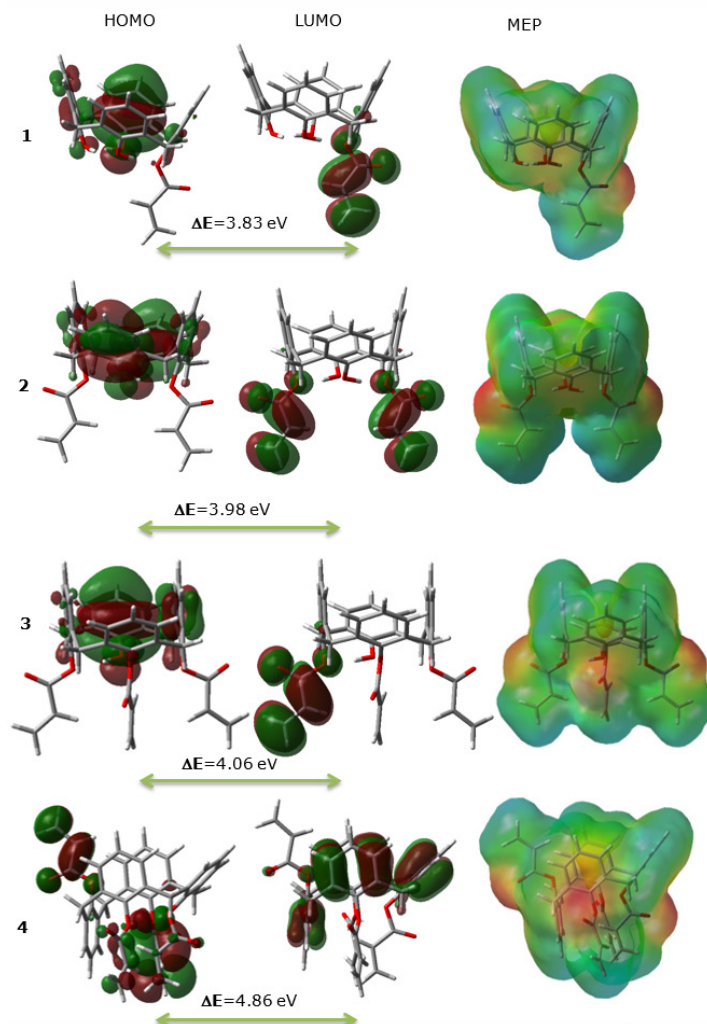
ΔE=3.98 eV

ΔE=4.06 eV

ΔE=4.86 eV

Figure 4. HOMO-LUMO and MEP drawing of the compounds.

molecular hydrogen bonding. In addition, it is only estimated that the conformational structure can be a Partial Cone or 1,3-Alternate due to the steric effect. However, the exact conformation was determined as Partial Cone by DFT method. It has been shown that molecules (1, 2 and 3) having hydroxyl group adopt Cone conformation, being most stable state, while Partial Cone is the lowest energy state for compound 4 without free phenolic groups. The robust O⁻H···O type bonds of 1, 2 and 3 compounds have given rise to be planarity of the molecules. In NBO analyses, it is understood that the LP → σ* interactions for O···O⁻H IHBs and the delocalization LP → π* for O⁻C=O are the major contributions to energy stabilization. The determination of accurate structures as a result of laborious conformational search will shed light on understanding of host-guest mechanisms of Calix[4] arene molecules.

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