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 Calixararene 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.

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).

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-
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 H-bonds 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 1. The structures of Calix[4]arene derivatives including acryloyl moiety.](image1)

![Figure 2. All possible conformers of Calix[4]arene derivatives including acryloyl moiety.](image2)
motions, 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 hydrogen bonding.

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

| Comp. | Conformer   | $E$ (hartree) | $\Delta E$ kcal/mol |
|-------|-------------|---------------|---------------------|
| 1     | Cone        | -1573.1375732 | 0.0                 |
|       | Partial cone| -1573.1275896 | 6.26               |
|       | 1,2-Alternate| -1573.121664  | 10.01              |
|       | 1,3-Alternate| -1573.1214976 | 10.09              |
|       | Experimental| -1568.8625973 | 0.0                |
| 2     | Cone        | -1763.8625073 | 0.0                |
|       | Partial cone| -1763.8613754 | 0.71               |
|       | 1,3-Alternate| -1763.872664  | 3.29               |
|       | 1,2-Alternate| -1763.8536385 | 5.57               |
| 3     | Cone        | -1954.5940627 | 0.0                |
|       | Partial cone| -1954.593894  | 0.11               |
|       | 1,3-Alternate| -1954.5922281 | 1.15               |
|       | 1,2-Alternate| -1954.5911824 | 1.82               |
| 4     | Partial cone| -2145.326822  | 0.0                |
|       | 1,3-Alternate| -2145.3282442 | 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).

| Table 2. Hydrogen-bond geometries (Å, °) of compound 1, 2 and 3. |
|-------------------|-------------------|-------------------|-------------------|
| Molecule          | $D$—$H$—$A$       | $D$—$H$           | $H$—$A$          | $D$—$H$—$A$       |
| 1 Model optimization | 1.741 2.687 161.2  | 1.729 2.686 169.2  | 1.800 2.773 173.3  | 1.878 2.843 173.5  |
| 1 Experimental$^b$ | 2.00 (11) 2.897 (3) 170 (9)  | 2.11 (8) 2.855 (4) 157 (8)  | 1.97 2.843 173.5  | 1.893 2.852 169.4  |
| 2 Exp_optimization | 1.878 2.843 173.5  | 1.878 2.843 173.5  | 1.893 2.852 169.4  | 1.893 2.852 169.4  |
| 3 Model_optimization | 2.024 2.975 166.6  | 2.024 2.975 166.6  | 2.024 2.975 166.6  | 2.024 2.975 166.6  |

$^b$These results were taken from literature (10).
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. Accor-
ding to Column ∆E 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 unders-
tood 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-
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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**References**

1. Gutsche CD. Calixarenes Revisited, The Royal Society of Chemistry, Cambridge, UK, 1998.
2. Furer VL, Potapova LI, Vatsouro IM, Kovalev VV, Shokova EA, Kovalenko VI. Investigation of the conformation and hydrogen bonds in adamantylcalix[4]arene by IR spectroscopy and DFT. Journal of Molecular Structure 1171 (2018) 207-213.
3. Şener I, Şener N, Erişkin S. Synthesis and absorption spectra of...
some novel hetaryltraksazocalix[4]arene derivatives. Dyes and Pigments 96(1) (2013) 256–263
4. Galindo-Murillo R, Olmedo-Romero A, Cruz-Flores E, Petrar PM, Kunsagi-Mate S, Barroso-Flores J. Calix[n]arene-based drug carriers: A DFT study of their electronic interactions with a chemotherapeutic agent used against leukemia. Computational and Theoretical Chemistry 1035 (2014) 84–91.
5. Shamova LI, Shamov GA, Antipin IS, Konovalov AI. Modeling K + and Ag + Complexation by Thiocalix[4]arene Amides Using DFT: The Role of Intramolecular Hydrogen Bonding. The Journal of Physical Chemistry A 113 (19) (2009) 5691–5699.
6. Bifulco G, Gomez-Paloma L, Riccio R, Gaeta C, Troisi F, Neri P. Quantum Mechanical Calculations of Conformationally Relevant 1 H and 13 C NMR Chemical Shifts of Calixarene Systems. Organic Letters 7(26) (2005) 5757–5760.
7. Guzzo RN, Rezende MJC, Kartnaller V, Carneiro JW de M, Stoyanov SR, Costa da LM. Experimental and DFT evaluation of the 1H and 13C NMR chemical shifts for calix[4]arenes. Journal of Molecular Structure 1157 (2018) 97-105.
8. Kostyukevych KV, Khristosenko RV, Pavluchenko AS, Yakhula AA, Kazantseva ZI, Koshets IA, Shirshov YM. A nanostructural model of ethanol adsorption in thin calixarene films. Sensors and Actuators B: Chemical 223 (2016) 470–480.
9. Özkınalı S, Kocakutken H, Synthesis, spectral characterisation and thermal behaviours of some new p-tert-butylicalix[4]arene and calix[4]arene-esters containing acryloyl groups. Journal of Molecular Structure 1033 (2013) 70–78.
10. Özkınalı S, Uçar İ, Kocakutken H, Bulat A. 25,27-Bis(acryloyloxy)-26,28-dihydroxyicalix[4]arene toluene hemisolvate. Acta Crystallographica Section E Structure Reports Online 63(8) (2007) o3378–o3378.
11. Roy D, Todd K, John M. GaussView, Version 5, Semichem Inc., Shawnee Mission, KS, 2009.
12. Walters P, Stahl M, Babel, Version 1.1, Department of Chemistry, University of Arizona, Tucson, AZ 85721.
13. Frisch MJ, Trucks WG, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JA Jr., Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Keith T, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam JM, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas O, Foresman JB, Ortiz JV, Cioslowski J, and Fox DJ. Gaussian 09, Revision C.01, Gaussian, Inc., Wallingford CT, 2010.
14. Glendening ED, Reed AE, Carpenter JE, Weinhold F. NBO Version 3.1, TCI, University of Wisconsin, Madison, 1998.
15. Özkınalı S, Karayel A. Synthesis, characterization, conformational equilibrium and intramolecular hydrogen bond analysis of Novel Azocalix[4]arenes including acryloyl moiety using DFT studies. Journal of Molecular Structure 1176 (2019) 303–313.
16. Chawla HM, Singh SP, Sahu SN, Upreti S. Shaping the cavity of calixarene architecture for molecular recognition: synthesis and conformational properties of new azocalix[4]arenes. Tetrahedron 62(33) (2006) 7854–7865.