CONFORMATIONAL EQUILIBRIUM AND SPECTROSCOPIC PROPERTIES OF CALIX[4]ARENE: THEORETICAL STUDY USING *AB INITIO* METHOD

Hanggara Sudrajat * and Ria Armunanto

Austrian-Indonesia Centre for Computational Chemistry, Department of Chemistry,
Faculty of Mathematics and Natural Sciences, Gadjah Mada University, Sekip Utara Yogyakarta 55281

ABSTRACT

Molecular structures were optimized for the calix[4]arene by ab initio method at the Hartree-Fock level of theory using LANL2DZ and 6-311G basis sets. Conformational equilibrium of four calix[4]arene conformers are reported. The results are compared with experiment, force field, and semiempirical molecular orbital calculations. General trends in relative stabilities of calix[4]arene decrease in following order: cone > partial-cone > 1,2-alternate > 1,3-alternate. The most stable conformer is the cone conformer that is stabilized by an array of four hydrogen bonds and this result agree with the reported experimental observations. All structures were analyzed using theoretical IR, UV-Vis, and ^{1}H NMR spectra attributed to the conformational equilibrium at the Hartree-Fock level of theory using LANL2DZ basis set.

INTRODUCTION

A wide variety of macrocyclic ligands able to interact with cations, anions, and neutral species are known. These have been isolated from natural resources or are the result of the synthetic developments which have taken place in the last 30 years [1-2]. Among the latter, calixarenes (products of the base-induced condensation of *p*-substituted phenols and formaldehyde) and their derivatives have received considerable attention in recent years. There are several reasons for the current widespread interest in calixarenes. An important one is the remarkably simple way (single-step procedure) used for the synthesis of the parent compounds. In addition, lower and upper rim functionalization of these macrocycles has resulted in a massive expansion in the range of derivatives available [3-5]. Within this context, calix[4]arenes are of particular interest.

Calix[4]arenes are macrocyclic compounds which are increasingly being used as building blocks in supramolecular chemistry [6-10]. One interesting property of calix[4]arenes is that they can exist in four ex

treme conformations, designated cone, partial-cone, 1,2-alternate, and 1,3-alternate. Although each phenol unit can rotate according to the oxygen-through-the-annulus rotation mechanism, they favorably adopt a cone conformation because of stabilization by intramolecular hydrogen bonding interactions among OH groups [11].

The investigation on the structural and energetic of calix[4]arene and it's derivatives has been the subject of numerous works. Several studires have been reported in which the relative stability of the calix[4[arene conformations are determined by experiments and theoretical calculations methods. Although the reduction to a small number of conformers simplifies considerably the task of modeling calix[4]arene by theoretical calculations, the size of the system makes a full first-principles approach difficult. Consequently, a significant number of works on these systems has been based on force field [12-16], or semiempirical molecular orbital approaches [12,16-17].

In the present work we report *ab initio* results for the structure and conformational equilibrium. Our aim is to provide accurate theoretical information on the conformational equilibrium of this molecule by *ab initio* calculation. We are also analyzed for the structure of the calix[4]arene conformers using IR, UV-Vis, and ^{1}H NMR spectra at the Hartree-Fock level of theory using LANL2DZ basis set.

COMPUTATIONAL METHODS

The initial structures of calix[4]arene were constructed by HyperChem 7.5 program[18]. In order to find optimized conformations, we executed conformational search by MM/MD simulation. The struc
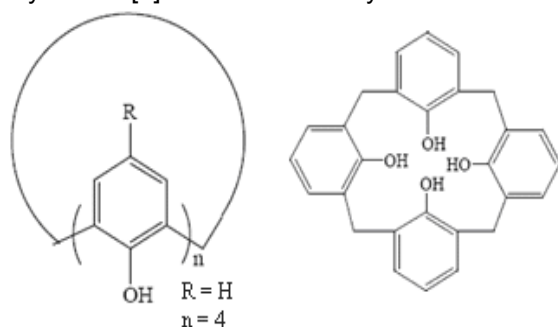

Figure 1. Chemical structure of calix[4]arene

* Corresponding author. Tel/Fax : +62-274-517656
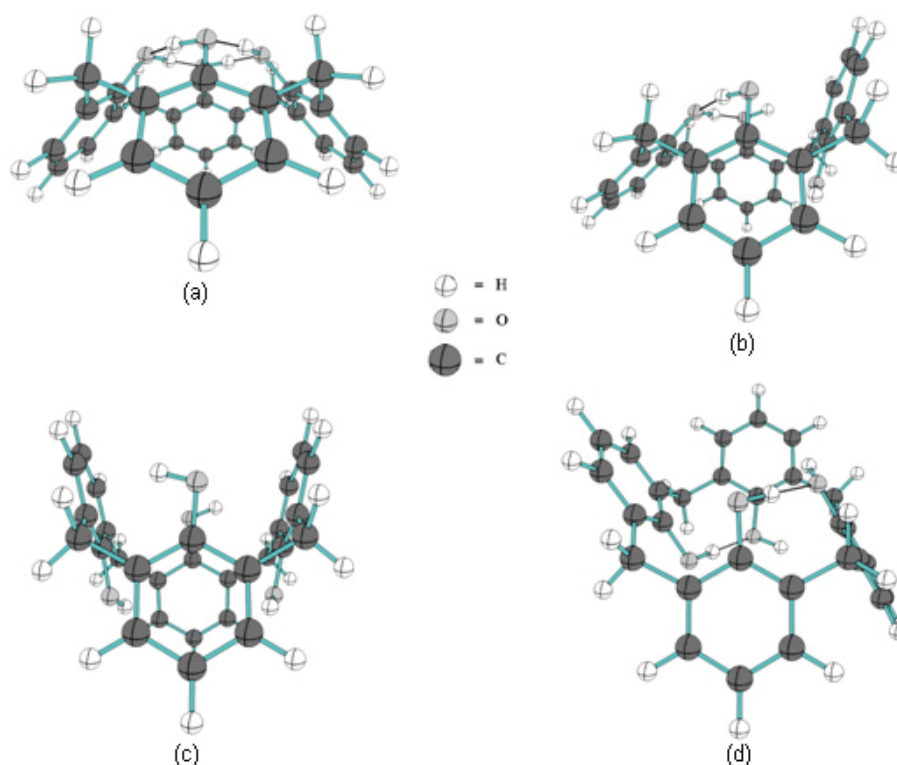Email address : angga_vanniveau@yahoo.com

Figure 2. Calix[4]arene conformers. (a) cone, (b) partial-cone, (c) 1,3-alternate, (c) 1,2-alternate
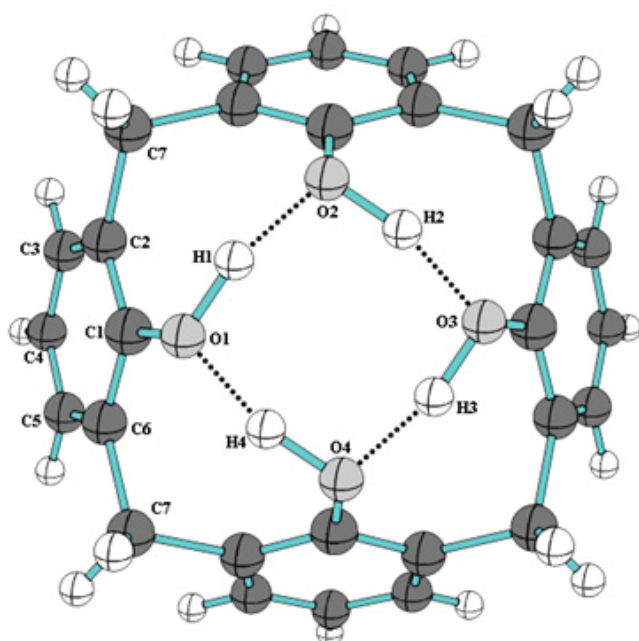

Figure 3. Hydrogen bonding in the calix[4]arene cone conformer

tures of calix[4]arene obtained from MM/MD calculations were fully re-optimized using *ab initio* methods to estimate the absolute and relative energies for the different conformations.

We have carried out geometry optimizations at Hartree-Fock level of theory using LANL2DZ and 6-311G basis sets. The calculations have been performed with the GAUSSIAN 98 program [19]. For comparison with other theoretical approaches, results based on AM1 [20], PM3 [21], CHARMM [22], MM3 and MM+ [23] are also reported. We calculated IR, UV-Vis, and ^{1}H NMR spectra at the Hartree-Fock level of theory using LANL2DZ basis set.

RESULT AND DISCUSSION

Conformational Equilibrium

Figure 2 shows the structure of the four calix[4]arene conformers. Figure 3 illustrates hydrogen bonding in the cone conformer. The total energy of the cone conformer and the energy differences between the others conformers are reported in Table 1. All the calculations predict that the most stable conformer is the cone conformer that is stabilized by an array of four hydrogen bonds.

Comparison of HF/LANL2DZ and HF/6-311G results indicate that by using different basis set, the cone conformer is significantly stabilized relative to all others conformers. Thus, the energy differences between partial-cone and cone conformer changes from 12.1 kcal/mol at HF/LANL2DZ to 10.7 kcal/mol at HF/6-311G. In addition, at HF/6-311G, the relative stability of conformers 1,2-alternate and 1,3-alternate is inversed when compared to HF/LANL2DZ results. However, all calculations predict that the energy differences between these conformers (1,2-alternate and 1,3-alternate) is very low (≈ 1 kcal/mol).

Indo. J. Chem., 2008, 8 (3), xx - xx

399

Table 1. Total energies of the cone calix[4]arene conformer at different theoretical level

Methods	Cone (a.u)	Partial-cone [a]	1,2-alternate [a]	1,3-alternate [a]
HF/LANL2DZ	-1373.42	12.1	20.4	20.9
HF/6-311G	-1373.53	10.7	18.6	18.1
AM1		7.4	10.4	11.5
PM3		7.4	12.4	11.1
CHARMM		9.6	11.8	17.2
MM3 (89)		9.9	11.7	18.7
MM3 (92)		5.6	6.1	10.6
MM$^+$		7.4	9.3	13.6
experiment [b]		14.9 [c] ; 13.8 [d]		

[a]Energy differences (ΔE's in kcal/mol) between the conformers (Partial-cone, 1,2-alternate, 1,3-alternate and the cone conformer. [b]From ref [24], [c]in chloroform, [d]in benzene

Table 2. Data for the structure of cone calix[4]arene

Parameters	HF/LANL2DZ	HF/6-311G	AM1	experiment [a]
Bond distances (Å)				
C_1-C_2	1.41	1.41	1.41	1.41
C_1-C_6	1.40	1.40	1.40	1.40
C_2-C_3	1.39	1.39	1.40	1.39
C_2-C_7	1.53	1.53	1.50	1.53
C_1-O	1.41	1.42	1.38	1.41
O-O	2.65	2.64	2.91	2.64
Angels (deg)				
C_1-C_2-C_3	117.3	117.3	114.3	117.3
C_1-C_2-C_7	122.1	122.1	122.7	121.9
C_1-C_6-C_7	121.1	121.0	121.4	120.8
C_2-C_7-C_6	113.1	113.1	111.4	113.0
C_2-C_1-C_6	121.7	121.8	121.2	121.6
O_1-C_1-C_2	119.7	119.7	123.0	119.1
O_1-C_1-C_6	117.4	117.4	115.8	117.8

[a]From ref [25]

Comparison with experimental data is not direct since the available data is from measurements in the liquid phase and solvent effects can be important. Experimental free energies of activation (ΔG) for conformational inversion of calix[4]arene in two different solvents (*i.e.* in chloroform and in benzene) [26] are reported in Table 1.

Table 1 also presents results for the energy differences between the calix[4]arene conformers based on force field and semiempirical molecular orbital calculations. Similar values for the energy differences between the partial cone and cone conformers and also between 1,3-alternate and cone are predicted by force field calculations (CHARMM and MM3). However, semiempirical molecular orbital predict a very low energy difference between 1,2-alternate and 1,3-alternate conformers (less than 1 kcal/mol), which disagrees significantly with force field results (≈4-6 kcal/mol). Apparently, this disagreement is not related with significant differences in the structures.

Among various methods reported in Table 1, HF/LANL2DZ method gives result for the energy differences between the calix[4]arene conformers that energetically close with experimental value. Therefore,

HF/LANL2DZ method presumably is the best method for determination of structural and spectral properties of calix[4]arene.

Structure

Table 2 reports structural information from experiment, *ab initio* method, and semiempirical molecular orbital theory (AM1). The experimental data are from the hexagonal phase of the calix[4]arene-acetone clathrate. Although condensed phase structures are not directly comparable to gas phase data, our predictions based on *ab initio* optimizations are in very good agreement with experiment. We found that O-O distance calculated by *ab initio* is in perfect agreement with experiment. We interpret the agreement between our *ab initio* results and experiment as a strong indication that the present approach is adequate to correctly describe the structure of calix[*n*]arenes. AM1 results for the structural parameters of the cone calix[4]arene are in good agreement. One exception is the O-O distance calculated by *ab initio* (2.64 Å) that is much shorter than AM1 (2.9 Å).

Table 3 reports data on the structure of the cone conformer of calix[4]arene. We have restricted our dis cussion to the structural parameters related to hydrogen bonding in the lower rim of calix[4]arene. For the cone conformer we can observe a significant reduction of the O-H bonds (H_1-O_2, H_2-O_3, H_3-O_4, H_4-O_1) when we move from HF/LANL2DZ to HF/6-311G. This dependence suggests that different basis set effects contributes to significantly reduce the O-H bond lengths.

Table 3. Structural data related to hydrogen bonding for the cone conformer

Parameters	HF/LANL2DZ	HF/6-311G
	Bond distances (Å)	
O_1-H_1	1.026	1.038
H_1-O_2	1.401	1.761
O_2-H_2	1.026	1.038
H_2-O_3	1.401	1.761
O_3-H_3	1.026	1.038
H_3-O_4	1.401	1.761
O_4-H_4	1.026	1.038
H_4-O_1	1.401	1.761
	Angels (deg)	
O_1-H_1-O_2	165.402	161.443
H_1-O_2-H_2	104.132	104.904
O_2-H_2-O_3	165.479	161.433
H_2-O_3-H_3	104.132	104.903
O_3-H_3-O_4	165.454	161.454
H_3-O_4-H_4	104.132	104.903
O_4-H_4-O_1	165.421	161.453
H_4-O_1-H_1	104.132	104.903

Infrared spectra

One of the particulary distinctive features of the calixarenes is the unusually low frequency at which the stretching vibration of the OH groups occurs in the infrared, ranging from *ca*. 3150 cm^{-1} for the cyclic tetramer to ca. 3300 cm^{-1} for the cyclic pentamer., with the other calixarenes falling in between these extremes. This is the result of the especially strong intramolecular hydrogen bonding that exists in these molecules. 'Circular hydrogen bonding' undoubtedly is responsible for some of the unique features of the calix[4]arene. Subtle changes in the shape of the hydrogen bond array can alter the strengths of the hydrogen bonding.

The theoretical IR spectra for the calix[4]arene in four conformers is shown in Figure 4. For all spectra show strong peak at *ca*. 3415 cm^{-1} correspond to the streching vibration of the OH groups. The 1,3-alternate isomers have lowest OH stretching frequency due to the absence of intramolecular hydrogen bonds. In the cone conformer, four hydrogen bonding occur, thus, the strengths of the hydrogen bonding increase (*i.e.* decreasing υ_{OH} value). To directly compare with experimental data, the calculated frequencies were scaled following the recommended scale factor of 0.893 [26]. The obtained OH stretching frequencies (*i.e.*: 3040 cm^{-1}, 3043 cm^{-1}, 3070 cm^{-1}, 3064 cm^{-1} for cone, partial-cone, 1,3-alternate, and 1,2-alternate conformers, respectively) are very close with previous experimental values.
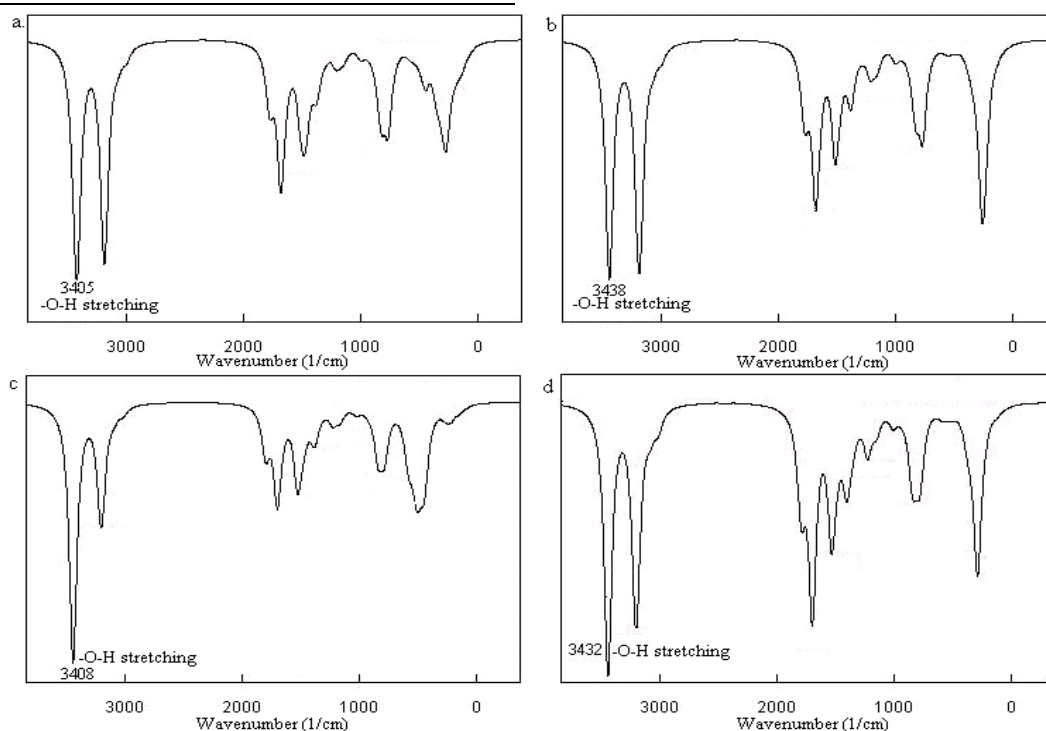

Figure 4. Calculated IR spectra of calix[4]arene conformers. (a) cone, (b) 1,3-alternate, (c) partial-cone, (d) 1,2-alternate
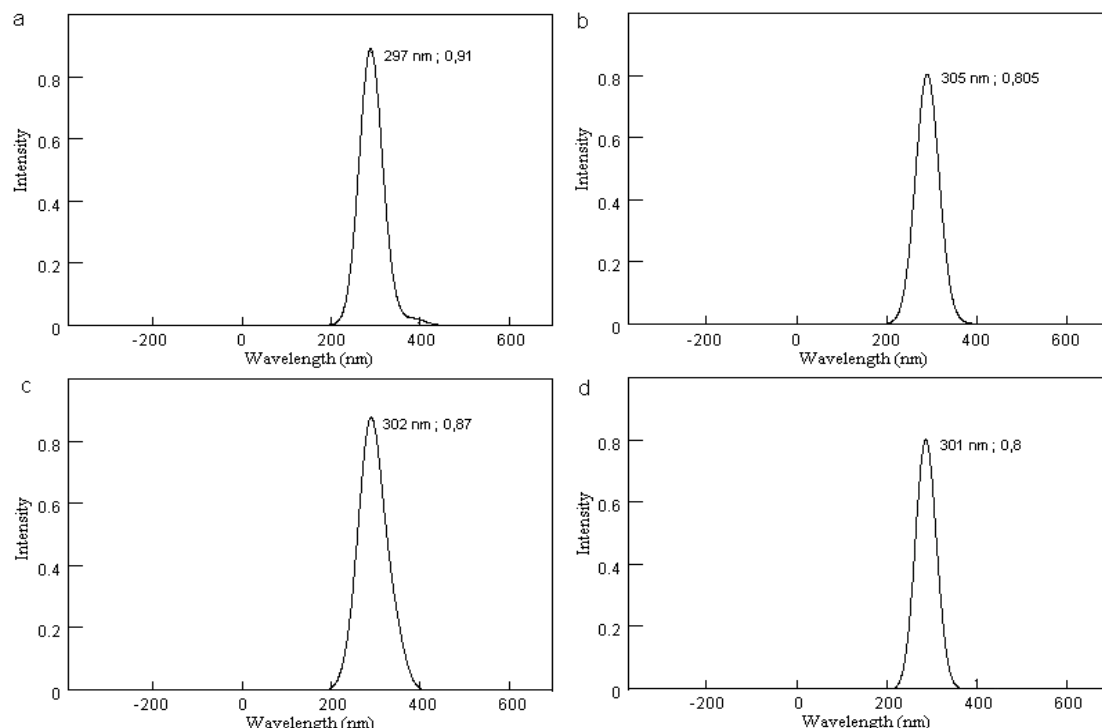
Figure 5. Calculated UV-Vis spectra of calix[4]arene conformers. (a) cone, (b) 1,3-alternate, (c) partial-cone, (d) 1,2-alternate

The high frequencies of the non-interacting CH stretching above 3000 cm^{-1}. On the other hand, the frequencies around 1450 cm^{-1} correspond to the CC stretching motions of the benzene rings. In the fingerprint region the calix[4]arenes conformers all look rather similar to one another, especially between 1600 and 900 wavenumbers. In the 500-900 cm^{-1} region, however, the patterns vary to some extent.

UV-Vis spectra

The theoretical UV-Vis spectra for the calix[4]arene in four conformers is shown in Figure 5. All conformer have a single absorption maxima at *ca*. 300 nm in the ultraviolet region. We found that this results is in agreement with experimental values (*ca*. 288 nm). For all conformers of calix[4]arene, cone conformer showed the most pronounced absorption maxima at most low wavelength. This results indicated that cone conformer is most stable structure due to the highest first ionization energy.

^{1}H-NMR spectra

The theoretical ^{1}H-NMR spectra for the calix[4]arene in four conformers is shown in Figure 6. The results showed that for the cone conformer, the Ar-CH$_2$-Ar protons signals gives a pair of doublets, partial-cone conformers gives a pair of doublets and one singlets, 1,2-alternate conformer gives two pair of doublets and one singlets, 1,3 alternate gives one singlets. The resonance for the aromatic protons for the cone conformer are singlets, partial-cone conformers gives one singlets, 1,2-alternate conformer gives a pair of doublets and one singlets, 1,3 alternate gives one singlets. The position of singlet arising from the OH groups varies with the conformers of the calix[4]arene and does not correlate particularly well with the strength of hydrogen bonding as judge by υ_{OH} frequencies in the IR spectra. The obtained ^{1}H-NMR spectra is in agreement with the experimental values.

CONCLUSION

This work reports *ab initio* calculations for an important and complex molecule that is presently a model system in host-guest chemistry. We have compared our predictions for the conformational equilibrium with theoretical results based on force field and semiempirical methods. *Ab initio* calculations suggest that the relative stability of the different conformers of calix[4]arene is in following order: cone > partial-cone > 1,2-alternate > 1,3-alternate. Our results also suggest that the energy difference between 1,2 alternate and 1,3-alternate conformers of calix[4]arene is overestimated by force field calculations. *Ab initio* results for the structure of the cone calix[4]arene conformer are in very good agreement with experimental data. However, some discrepancies are found when we compare AM1 predictions with experimental data.
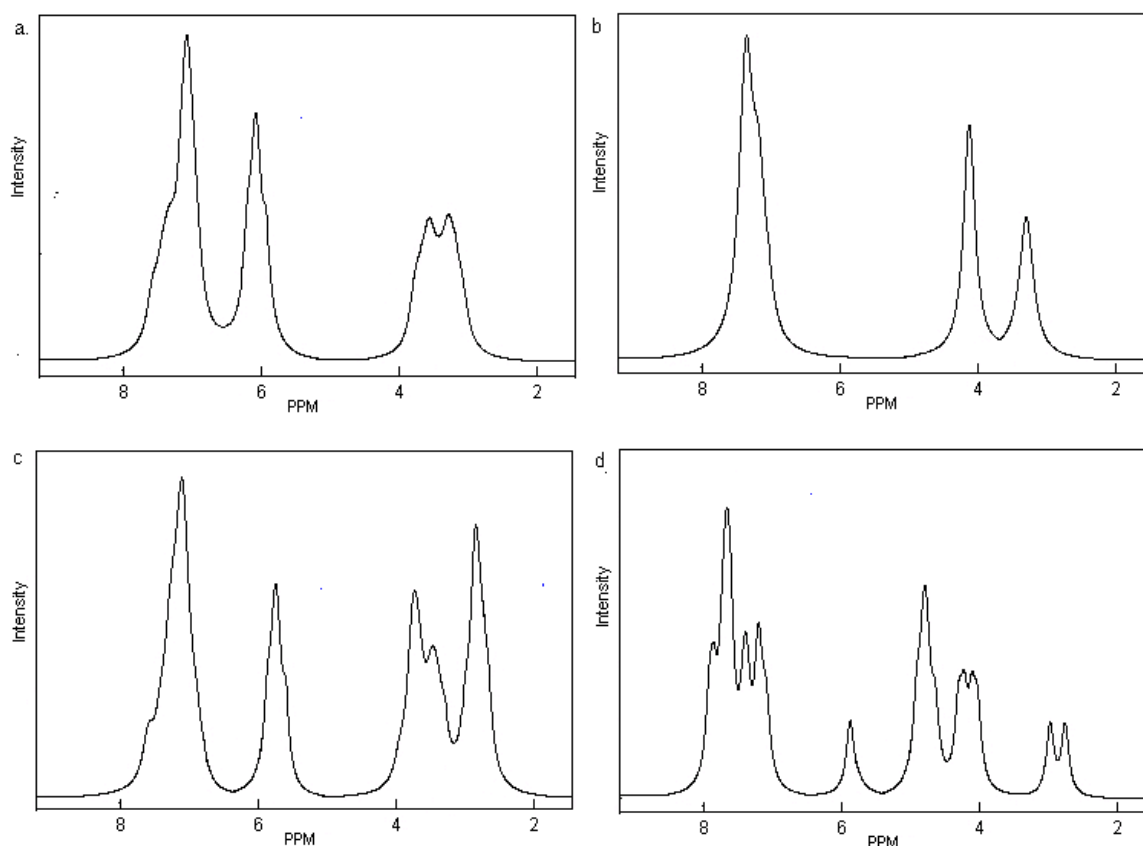
Figure 6. Calculated ^{1}H-NMR spectra of calix[4]arene conformers. (a) cone, (b) 1,3-alternate, (c) partial-cone, (d) 1,2-alternate

The calculated IR, UV-Vis, ^{1}H NMR, and ^{13}C NMR spectra results agree well with the structural features of the molecules. The diagnostic differences in the all spectra should provide us the key to understand more deeply the host-guest molecular structures by enabling to assign and distinguish the individual molecular states.

ACKNOWLEDGEMENT

REFERENCES

1. Lehn, J.M., 1995, *Supramolecular Chemistry*; VHC: Weinheim, Germany, 243-247.
2. Cox, B.G., and Schneider, H., 1992, *Coordination and Transport Properties of Macrocyclic Compounds in Solution*; Elsevier: Amsterdam, 307-310.
3. Bohmer, V., 1995, *Angew. Chem., Int. Ed. Engl.* 34, 713.
4. Neri, P., Geraci, C., and Piatelli, M, 1995, *J. Org. Chem,* 60, 4126
5. van Dienst, E., Iwema, B.W.I., Engbersen, J.F.J., Verboom, W., and Reinhoudt, D.N., 1993, *Pure Appl. Chem, 65*, 387.
6. Gutsche, C. D., 1989, *Calixarenes*; Royal Society of Chemistry: Cambridge, 143-145.
7. Ikeda, S., and Shinkai, A., 1997, *Chem. Rev.*, 97, 1713-1734.
8. Alemán, C., den Otter, W.K., Tolpekina, T.V., and Briels, W.J., 2003, *J. Org. Chem.*, 69, 951-958.
9. Arnaud-Neu, F., Collins, E.M., Deasy, M., Ferguson, G., Harris, S.J., Kaitner, B., Lough, A.J., McKervey, M.A., and Marques, E., 1989, *J. Am. Chem. Soc.*, 111, 23, 8681-8691.
10 Chawla, H.M., and Singh, P., 2007, *Tetrahedron.*, 64, 4, 741-748.
11 de Namor, A.F.D., Cleverley, R.M., and Zapata-Ormachea, M.L., 1998, *Chem. Rev.*, 98, 2495-2525.
12 Grootenhuis, P.D.J., Kollman, P.A., Groenen, L.C., Reinhoudt, D.N., van Hummel, G.J., Ugozzoli, F., and Andreetti, G.D., 1990., *J. Am. Chem. Soc.*, 12, 4165-4176.

Indo. J. Chem., 2008, 8 (3), 397 - 403

403

13 Harada, T., Rudziński, J.M., and Shinkai, S., 1992, *J. Chem. Soc. Perkin Trans.*, 2, 2109-2115.

14 Harada, T., and Shinkai, S., 1995, *J. Chem. Soc. Perkin Trans.*, 2, 2231-2242.

15 Fischer, S., Grootenhuis, P.D.J., Groenen, L.C., van Hoorn, W.P., van Veggel, F.C.J.M., Reinhoudt, D.N., and Karplus, M., 1995, *J. Am. Chem. Soc.*, 117, 1611-1620.

16 Lipkowitz, K.B., and Pearl, G., 1993, *J. Org. Chem.*, 58, 6729-6736.

17 Broyere,E., Persoons, A., and Bredas, J.L., 1997, *J.Phys.Chem.*,101,4142

18 *HyperChem Release 7.5*; Hypercube, Inc.: Waterloo, Ontario,Canada, 2002.

19 Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., irzewski, V.G., Montgomery, J.A.,Jr., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui, Q., Morokuma, K., Malick, D.K., Rabuck, A. D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Baboul, A.G., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith,T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Challacombe, M., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Andres, J.L., Gonzalez, C., Head-Gordon, M., Replogle, E.S., Pople, J.A., 1998, *Gaussian 98,* Revision A.11.3, Gaussian, Inc., Pittsburgh, PA.

20 Dewar, M.J.S., Zoebisc, E.G., and Healy, E.F., 1985, *J. Am. Chem. Soc*, 107, 3902.

21 Stewart, J.J.P., 1989, *J. Comput. Chem*, 10, 209.

22 Brooks, R., 1983, *J. Comput. Chem*, 4, 187.

23 Allinger, N.L., Yuh, Y.H., and Lii, J.H., *J. Am. Chem. Soc.*, 111, 8551.

24 Gutsche, C.D., and Bauer, L.J., 1985, *J. Am. Chem. Soc.*, 107, 6052-6059.

25 Ungaro, R., Pochini, A., Andreetti, G.D., and Sangermano, F., 1984, *J. Chem. Soc.*, *Perkin Trans. 2*, 1979 – 1985.

26 Foresman, J.B, and Frisch, A., 1996, *Exploring Chemistry with Electronic Structure Methods*, 2nd Ed, Gaussian, Inc., Pittsburgh.