A Quantum Chemical Study on Recognition of Nitro-phenols by Calix[n]arenes

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Abstract

A PM3 calculation in vacuum of the inclusion complexation of *o*-, *m*-, *p*-nitro-phenol with calix[n]arenes is performed successfully. The pathways for inclusion process are described and the most probable structures of the 1:1 complex are sought through a potential energy scan. The energy differences between the inclusion complexes and the hosts, by calculation, show that the most stable complexation is calix[4]-*p*-nitro phenol and calix[6]-*m*-nitro phenol.

Introduction

Calix[n]arenes (CAL) are versatile host molecules for molecular recognition and supra-molecular assembly because they can readily introduce functional groups into the phenolic OH and their *para* positions can realize a wide variety of functions [1]. They have been widely investigated and used because of their complex forming properties [6–8], their derivatives are used as sensing components in ionic sensors [2–4], as extractants [5], and as artificial ion channels [9]. Therefore, for the understanding of the properties and the mechanism, it is reasonable to study their structures.

Molecular dynamics were used for the simulation of complexes of CALs and their derivatives [10, 11], as well as their conformational transitions [12, 13]. Vibrational spectra of some host–guest structures were also reported [14].

Recently, the theoretical studies concerning CAL molecules and/or their derivatives have mostly been restricted to host–guest interaction calculations using molecular mechanics [15], quantum chemical methods [16, 17], or hybrid approaches [18]. The calculation of the equilibrium geometries of the four thiacalix[4]arene conformers was also reported [19].

To our knowledge, articles concerning the recognition of nitro-phenols by calix[n]arenes (conformation and its stabilization energy were given) have not been published yet.

Calculation and methodology

The complexations of calixarenes with nitro-phenols were studied with PM3 semi-empirical method. PM3 has a highly computational efficiency that permits the modeling of large systems, which are beyond the capacity of *ab initio* methods. The precision is comparable to that of *ab initio* with medium-sized basis sets. PM3 also performs better than
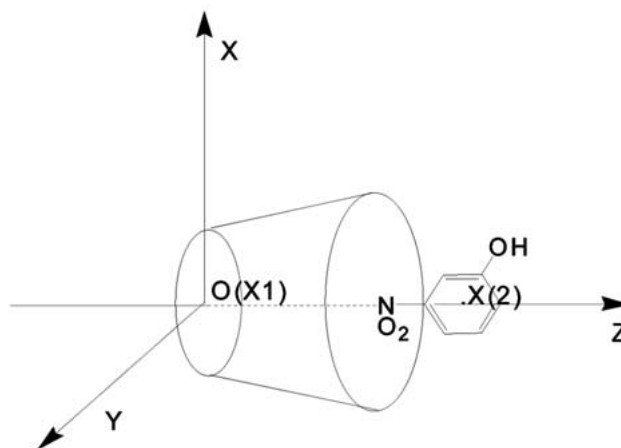

Figure 1. Coordinate system used to define the process of complexation of CAL with nitro-phenol.

AM1 in biochemical systems due to its improved description of interaction between non-bonded atoms. Hence, it is convenient to choose PM3 method to calculate our system [20].

All calculations were performed with *Gaussian 98* [21]. The initial structures of nitro-phenols were constructed and optimized with PM3 and HF/6-31G. Calixarenes were optimized with PM3 and HF/6-31G from their crystal structure [22], no geometry constraint was imposed on the optimization. The controlled reaction coordinate of the inclusion process is the distance between a dummy atom located at the center of hydroxyl groups of calixarene and a second dummy atom located at the center of benzene as illustrated in Figure 1. The upper rim of calixarene points toward the positive Z-axis. The inclusion complexation was emulated by introducing the guest molecule from one end of the CAL and letting it pass through the host molecule in steps. In each step, the geometry of the complex was fully optimized by PM3 without any restriction. As for calix[4]arene, since its cavity diameter is too small to hold a phenyl ring, the

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guest molecules cannot pass through the cavity but stays at the same place in every step. Several possible complexation orientations were considered. For simplicity, we called the orientation in which the nitro-substituent group of the guest pointed toward the center DX, while the other, XD. Frequency calculations using PM3 were performed to confirm the completeness of optimization, and no negative eigenvalues were found in the final structures.

Results and discussion

PM3 Geometry optimization

The energy changes in the inclusion process obtained several curves for these complexation orientations (Figure 2 and Table 1). The optimized structures at each energy minimum are shown in Figures 3 and 4.

The stabilization energies relative to the formation of each complex are listed in Table 2. The stabilization energy is calculated according to:

$$\Delta E = E_{(CAL:NP)} - E_{(CAL)} - E_{(NP)},$$

where $E_{(CAL:NP)}$ is the total energy of the host–guest complex, $E_{(CAL)}$, the energy of the free CAL molecule, and $E_{(NP)}$ the energy of the isolated nitro-phenol, respectively. It is obvious that CALs can form stable complexes with o-, m-, p-nitro-phenols.

From Figures 3 and 4, it can be seen that the conformations of nitro phenols are greatly affected during complexation. In calix[4]-nitro phenols, both the guests of m-nitro phenol and p-nitro phenol deviate from Z-coordinate, posing an angle of 14.3° and 15.6° respectively, and their oxygen atoms incline to the CAL wall. For calix[4]arene-o-nitro phenol, the guest still stays at Z-coordinate but its N—O axis inclines to the CAL wall, posing an angle of 12.2°. Similarly, in calix[6]-nitro phenol, the dihedral angles between nitro group and phenyl ring for m- and p-nitro phenols are −43.421° and −33.670°, respectively. As in calix[4]-o-nitro phenol, the dihedral angle between nitro group and phenyl ring for calix[6]-o-nitro phenol does not change but poses an angle of 32.4° between N—C axis and its Z-axis.

Complexation orientation

From Table 1, the XD orientation is more favorable than the DX one by an energy gap of 1.48 and 8.81 kJ/mol ($\Delta E = E_{(XD)} - E_{(DX)}$) in in calix[4]arene-$m$-nitro phenol and calix[4]arene-p-nitro phenol, respectively. But they from calix[4]arene-o-nitro phenol, in which the XD orientation is more favorable, having a −10.02 kJ/mol energy gap. This seemed inconsistent with m-, p-nitro phenol-CAL because all three nitro-phenols have the same group. They all have π-interactions and hydrogen interactions with the CAL host molecule. However, the present results are reasonable, for the OH···O bond distance of o-nitro phenol is 187.4 pm and there is an intra-molecular hydrogen bonding in the o-nitro phenol, which weakens the interaction between the

host–guest, and forms a very strong steric effect between the host–guest complexation of o-nitro phenol. Although van der Waals and hydrogen interaction considered in this paper dominate, other effects such as electrostatic effect may play an important role, since different charge distributions in o-, m-, p-nitro-phenols exist. The stabilization energy differences among the three complexes agree with the experimental observations, which also suggest that p-nitro phenol-calix[4]arene is the most stable one, followed by m-nitro phenol and o-phenol-calix[4]arenas [23].

Similarly, Table 2 shows that the DX orientation is more favorable than the XD one by an energy gap of 4.74 and 4.93 kJ/mol in calix[6]arene-m-nitro phenol and calix[6]arene-p-nitro phenol, respectively, and a 10.79 kJ/mol energy gap for calix[6]arene-o-nitro phenol in which the XD orientation is prevalent. As to their stabilization energy, the energy of calix[6]arene-m-nitro phenol complexation is larger than that of calix[6]arene-p-nitro phenol while calix[6]arene-o-nitro phenol is the least. These orientations are, probably, also caused by a subtle steric effect. In the DX orientation of calix[6]arene-m-nitro phenol, the phenyl ring of the guest is parallel to the other two phenyl rings of calix[6]arene. The four smallest distances separating nitro group and hydrogen of CAL are 254.6, 254.5, 263.3, and 255.8 pm, respectively. These values are more than the van der Waals radii, i.e., 240 pm in a way [24], which means that there is significant van der Waals attraction. On the other hand, there is a valuable interaction between the hydroxyl group of guest and two hydrogen of the CAL because their shortest distances are 346.3 and 355.8 pm. As discussed before in calix[4]arene complexes, different charge distribution may also influence the guest-host interaction. The same situation occurs in calix[6]-p-nitro phenol except for a longer distance between hydroxyl group of guest and hydrogen of calix. But this is not adaptable to the calix[6]-o-nitro phenol. As there is an intramolecular hydrogen bond between nitro group and the phenolic OH of o-nitro phenol, in its DX orientation, the distance between oxygen of guest and those of CAL is so small that the repulsion between these two would result in the increase of complexation energy. Comparing the results of the DX and XD orientations, PM3 calculation indicates that the more favorable conformation is one of the XD orientations.

Admittedly, the present calculation is only studied by semi-empirical (PM3) quantum chemical methods and only the gas-phase interaction for the bindings evaluated. This is the shortcoming of the current QM studies on CALs. Further study on the solution effect of CAL complexation is in progress.

Conclusions

The results of the quantum chemical calculations on the complexes formed upon recognition of o-, m-, p-nitro-phenol by calix[4]arene and calix[6]arene molecules were presented. The magnitude of the calculated stabilization energies indicated that p-nitro-phenol is the more tightly bonded amongst o-, m-, p-nitro-phenol molecules in
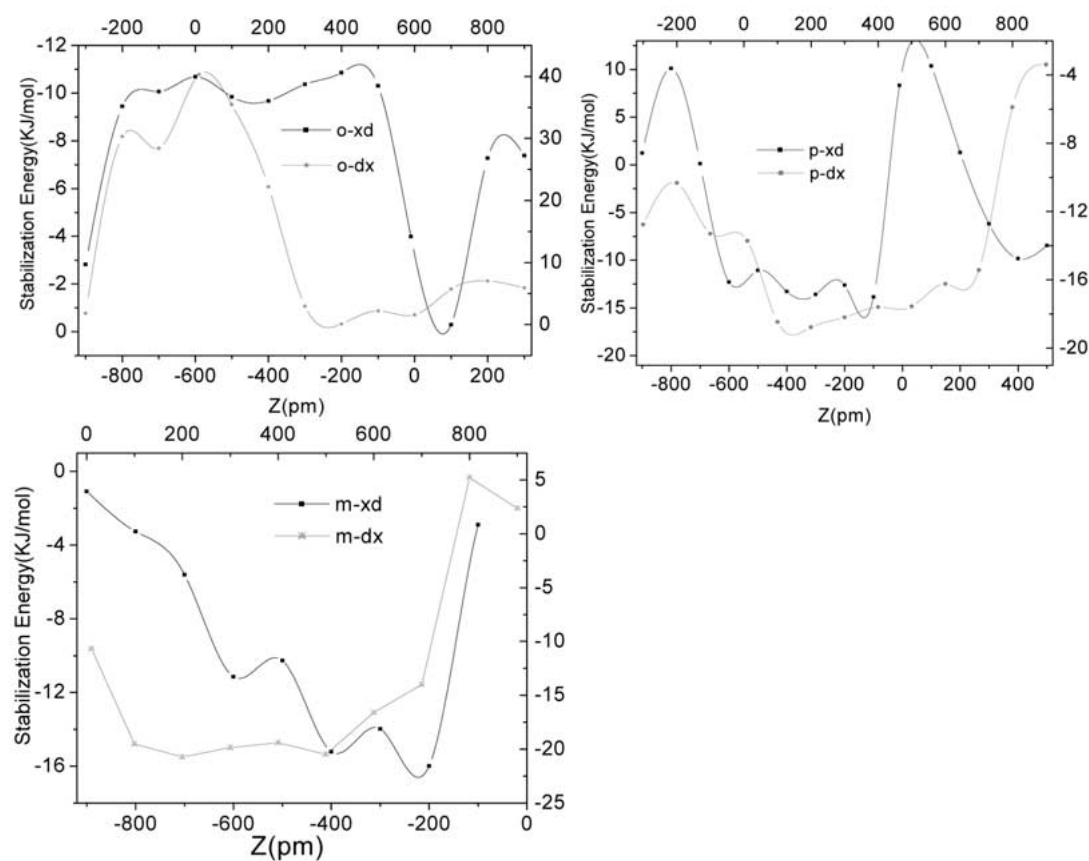
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Figure 2. Graphic diagrams for the emulation of inclusion complexation of nitro phenol into calix[6]arene. The position of the guest was determined by Z-coordinate of the N-atom from the center.

Table 1. Stabilization energy of calix[4]arene-nitro phenol, in some possible complexation orientations

| Z-axis | Stabilization energy (kJ/mol) | | | | | |
| | *o*-nitro phenol | | *m*-nitro phenol | | *p*-nitro phenol | |
	DX	XD	DX	XD	DX	XD
C—C	−10.17	−3.48	−11.95	−13.43	−6.93	−15.74
N—C	−13.28	−3.24	−1.82	−6.17		
O—C	−9.80	−3.82	−10.56	−6.14		
N—O					−1.84	−10.73

Table 2. Stabilization energy in inclusion complexation of calix[6]arene-nitro phenol (CAL: calix[6]arene; NP: nitro phenol)

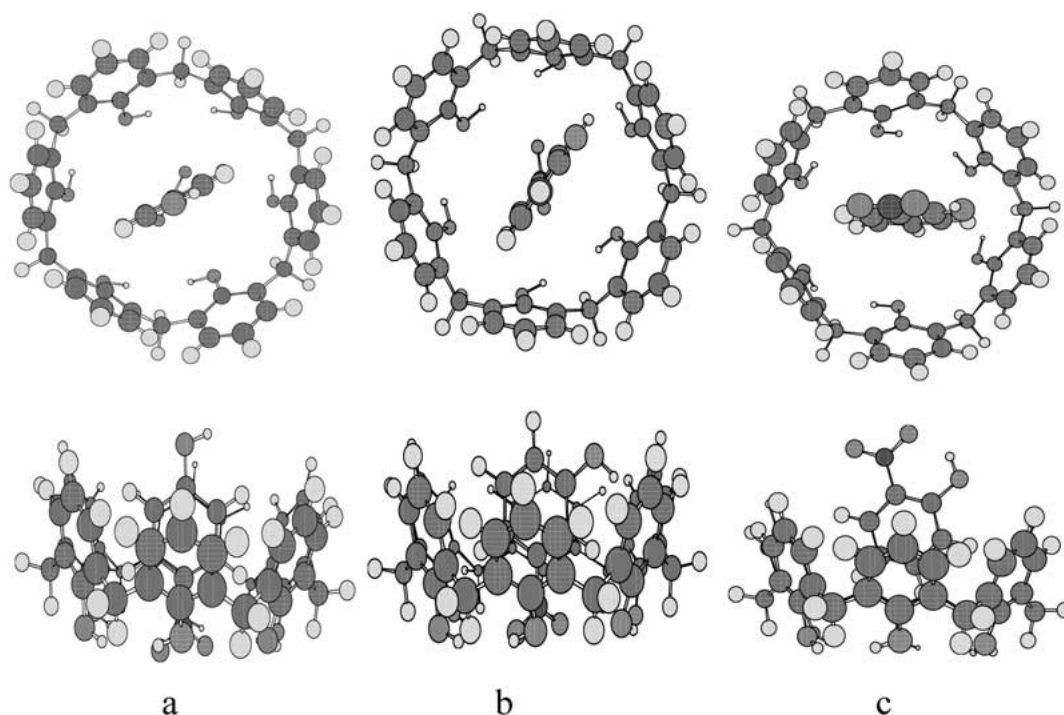| Species | CAL | *o*-NP | *m*-NP | *p*-NP | CAL-*o*-NP | | CAL-*m*-NP | | CAL-*p*-NP | |
					DX	XD	DX	XD	DX	XD
Heat of formation (kJ/mol)	−569.1	−139.7	−125.8	−133.2	−708.7	−719.7	−715.7	−710.9	−721.1	−716.2
Stabilization energy upon complexation (kJ/mol)					−0.1	−10.9	−20.7	−16.0	−18.8	−13.9

Figure 3. Structures of the energy minimum obtained by the PM3 calculations for calix[6]arene-nitrophenol complex (vertical view of the calix cavity (up) and side view (bottom)). (a) DX orientation of *p*-nitro phenol. (b) DX orientation of *m*-nitro phenol. (c) XD orientation of *o*-nitrophenol.
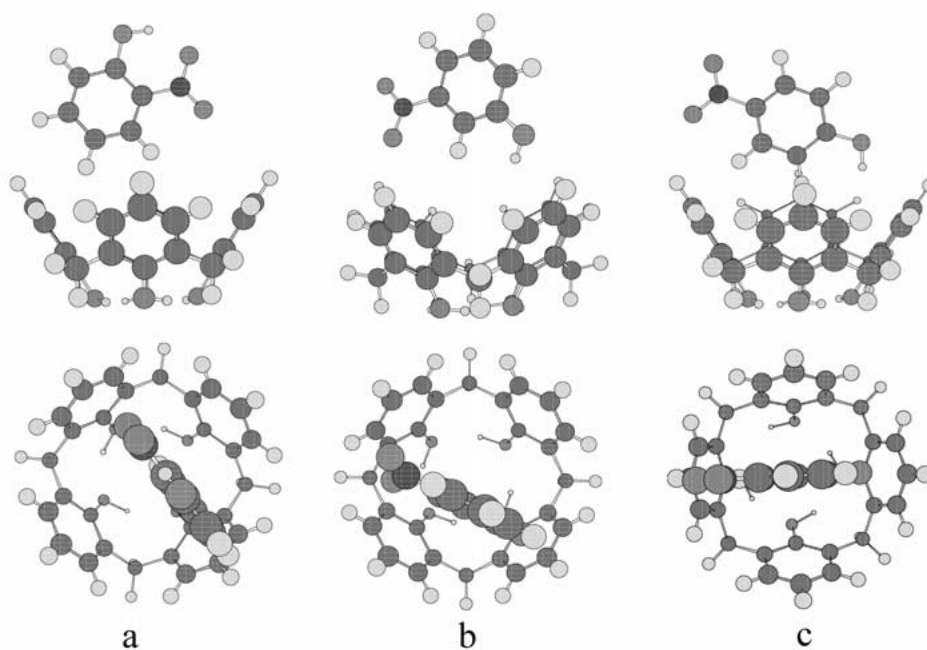

Figure 4. Structures of the energy minimum obtained by PM3 calculations for calix[4]arene-nitro phenol complex. Vertical view of the calix cavity (bottom) and side view (up). (a) Orientation of *o*-nitro phenol. (b) Orientation of *m*-nitro phenol. (c) Orientation of *p*-nitrophenol.

calix[4]arene herein investigated, followed by *m*-, *o*- nitro-phenols. This trend agrees with that of the experimental results. Different from the calix[4]arenes, in calix[6]arene-nitro phenols, the most stable complexation is calix[6]-*m*-nitro phenol and the complexation of *o*-nitro phenol is the least stable one.

The results presented herein may be useful for the study on recognition of CALs and on the separation of some aromatic compounds by CALs and their derivatives.

References

1. K. Chizuko, H. Yutaka, N. Tomohiro, H. Fumio, I. Nobuhiko, M. Naoya, and M. Sotaro: *J. Incl. Phenom. Macrocycl. Chem.* **42**, 89 (2002).
2. B.T.T. Lan and K. Toth: *Anal. Sci.* **14**, 191 (1998).
3. M. Shortreed, E. Bakker, and R. Kopelman: *Anal. Chem.* **68**(15), 2656 (1996).
4. S. O'Neill, P. Kane, M.A. McKervey, and D. Diamond: *Anal. Commun.* **35**, 127 (1998).
5. M.J. Schwing-Weill and F. Arnaud-Neu: *Gazzetta Chimica Italiana* **127**, 687 (1997).
6. M. Kubinyi, I. Mohammed-Ziegler, A. Grofcsik, I. Bitter, and W.J. Jones: *J. Mol. Struct.* **408/409**, 543 (1997).
7. I. Mohammed-Ziegler, M. Kubinyi, A. Grofcsik, A. Grun, and I. Bitter: *J. Mol. Struct.* **480/481**, 289 (1999).
8. I. Mohammed-Ziegler, B. Poor, M. Kubinyi, A. Grofcsik, A. Grun, and I. Bitter: *J. Incl. Phenom. Macrocycl. Chem.* **35**(1), 349 (1999).
9. L.S. Antipin, I.I. Stoikov, N.A. Fitseva, I. Stibor, and A.I. Konovalov: *4th International Conference on Calixarenes*, Parma, Italy, Book of Abstracts, pp. P80 and P131.
10. G. Wipff and M. Lauterbach: *Supramol. Chem.* **6**, 187 (1995).
11. N. Muzet, G. Wipff, A. Casnati, L. Dominiano, R. Ungaro, and F. Ugozzoli: *J. Chem. Soc. Perkin Trans.* **2**, 1065 (1996).
12. W.K. den Otter and W.J. Briels: *J. Chem. Phys.* **107**, 4968 (1997).
13. W.K. den Otter and W.J. Briels: *J. Am. Chem. Soc.* **120**, 13167 (1998).
14. F. Billes and I. Mohammed-Ziegler: *Supramol. Chem.* **14**5, 451 (2002).
15. W.P. van Hoorn, W.J. Briels, J.P.M. van Duynhoven, F.C.J.M. van Veggel, and D.N. Reinhoudt: *J. Am. Chem. Soc.* **63**, 1299 (1998).
16. I. Thondorf and J. Brenn: *Theochem.* **398**, 307 (1997).
17. B.P. Hay, J.B. Nicholas, and D. Feller: *J. Am. Chem. Soc.* **122**, 10083 (2000).
18. J. Golebiewski, V. Lamare, J.F. Dozol, M.T.C. Martins-Costa, C. Millot, and M.F. Ruiz-Lopez: *10th International Congress on Quantum Chemistry*, Menton, France (2000).
19. R.J. Bernardino and B.J. Costa Cabral: *6th International Conference on Calixarenes*, Enschede, The Netherlands, Book of Abstracts (2001), p. P13.
20. X.-S. Li, L. Liu, T.-W. Mu, and Q.-X. Guo: *Monatsh. Chem.* **131**, 849 (2000).
21. M. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, R.E. Stratmanm, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamao, S. Clifford, J. Ochterski, G.A. Pererson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabul, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle, and J.A. Pople: Gaussian 98, Revision A. 11, Gaussian Inc., Pittsburgh, PA (1988).
22. M.J. Huang, J.D. Watts, and N.S. Bodor: *J. Quantum Chem.* **64**, 711 (1997).
23. W. Xu, J.S. Li, Y.Q. Feng, S.L. Da, Y.Y. Chen, and X.Z. Xiao: *Chromatogr.* **48**(3–4), 245 (1998) and references therein.
24. F.A. Carey and R.J. Sundberg: *Advanced Organic Chemistry*, Part A, 3rd ed., Plenum Press, New York (1990), p. P130.