Quantum chemical investigations on bis(bora)calix[4]arene: a fluorescent fluoride sensor

Jae Hyeok Jin and Yoon Sup Lee[*]

Department of Chemistry, KAIST, Daehakro 291, Yuseong-gu, Daejeon, 305-701, Korea.

Tel: (042) 350-2861, **E-mail:** yslee@kaist.edu

Chemworks (or Chemworks2) ID: ecc13_kai_hyeok

ABSTRACT

The computational study on the fluoride ion binding with bis(bora)calix[4]arene has been performed using density functional theory and ONIOM model. The computed structure and fluorescent behavior of bis(bora)calix[4]arene was corresponded to experiment value. The binding energy for fluoride anion is computed to be 28.05kJ/mol in the chloroform solution. We also predicted that this sensing mechanism is only valid for fluoride ion in halogens. By analyzing molecular orbitals, binding with fluoride ion reduces energy differences between HOMO and LUMO, which leads to fluorescent sensing.

Key Words : Ab initio, Chemosensor, Calixarene, Bis(bora)calix[4]arene, Fluoride sensor, Density functional theory, ONIOM

Introduction

In the field of supramolecular chemistry and its application for biological procedure, a molecular sensor which derived from a molecular recognition phenomenon has received intense attention in the last years.[1] On account of this importance, considerable attention has been targeted on the calixarene-based molecules in these days which can act as a selective binder and carrier to facilitate to form a unique structure.[2] Especially treating upon these points and easiness of functionalization establishes a foothold to making artificial receptor. One of the applications for it is the synthesis of molecular sensor. In particular, synthesis of anionic molecular sensor is the case.[3]

Considering the mechanism as a sensor, the selective recognition of fluoride ion has been the subject of intensive research. It is of particular interest not only for dental care, osteoporosis, and fluorosis, but also the fluoride sensors appear to be attractive due to its simplicity, high sensitivity, and selectivity.[4]

Although some interesting sensing behavior about bis(bora)calix[4]arene with fluoride ion was reported, no calculations about both receptor interactions and sensing properties have been reported so far.[5] In fact, previous studies revealed only for the structure of calix-crown or calix-pyrroles, even with calixarenes for planar-like structures.

Herein we report the investigation of both interaction and sensing properties from *ab initio* computational point of view for this system. The main purpose of this article is threefold. Firstly, it is to provide the detailed optimized structure with more accurate method. Secondly, it is to give theoretical understanding of physical principles, which can be applied to act as a fluoride sensor. Finally, by using optimized structure, we can predict its mechanisms and further usability in other systems.

Theory and Computational Method

All calculations have been performed using Gaussian 09 code. Since previous studies revealed that the reliability of the B3LYP theory for fluorine calculations, we mainly use this theory to observe some

properties.[6]

Geometries have been optimized with using two layer ONIOM (Our-own-N-layer Integrated molecular Orbital+ molecular Mechanics) calculations.
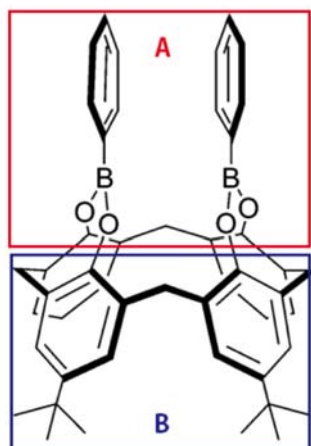

Figure 1. two layer ONIOM model for **1**

For the ONIOM calculations, we adjusted A as higher layer with B3LYP/6-31+G level, B as a lower layer with B3LYP/3-21G level. We set B as a lower level to calculate, because of high steric hindrance of t-butylbenzene and long distances from reaction site. The validity of this method was examined by NMR calculation.

After optimizing the geometry, single point energies of the geometry were fully evaluated with B3LYP/6-31+G level. To investigate the influence of solvents, we performed the polarized continuum model (PCM) calculations at the same level. (30, keynote)

In general, basis set superposition error should be considered to obtain an accurate interaction energy.[7] However, in our article, it is expected to be negligible compared to interaction energy since the reaction between **1** and F. involves lewis acid-base reaction.

To understand local electron density, especially for hydrogen, we have been performed NMR calculations. It has been reported that the method using the hybrid density functional theory with MPW91PW91 functional with 6-31+G is well suitable for calixarene and calixpyrrole system.[8] Therefore, we have been used this method for **1** and **1F** to figure out the significant shifts of hydrogen.

Absorption and fluorescent properties of **1F** have been predicted using the TD-DFT method at cam-B3LYP/3-21G level based on the optimized geometries, respectively.

Results and Discussion

Geometry Optimization of bis(bora)calix[4]arene

The B3LYP/ONIOM-optimized structure of **1** is represented in **Figure 2**. The distances between two borons are 3.621 angstroms, and the dihedral angle of two benzene rings is about 95°. The space filling model of DFT-optimized structure of the **1** indicates even if two boron atoms are spaced about 3.6 angstroms, there is no space for fluoride to form a bond. To receive fluoride anion, benzene rings must bent to make an extra space.
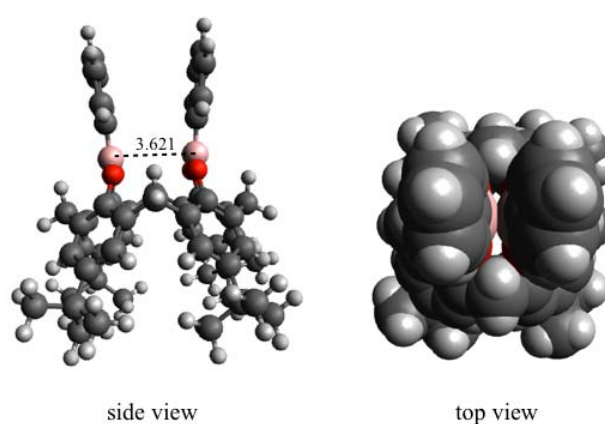

side view   top view

Figure 2. Optimized structure of **1** at the B3LYP/6-31+G:B3LYP/3-21G level.

To figure out the effect of solvent, we optimized **1** in acetonitrile at same level and slight differences were observed. Bond length between two borons are 3.660 angstroms and two benzene rings are located with 95.2°. The increasing boron-boron length and dihedral angle can be explained by the solvation effect. In this case, acetonitrile locates within the molecule to stabilize **1** by coulomb attraction.

Further, an interesting result can be obtained by performing population analysis of **1**. Results of the Mulliken charge calculations are followed by **Table 1**.

Mulliken Charge	Gas phase	Acetonitrile	Chloroform
Boron	1.030	0.958	0.960

Table 1. Calculated charge for boron in **1**

The positively charged boron atom is capable of interacting with fluoride anion. The interaction between boron and fluoride also explained as LUMO of **1,** which is depicted in **Figure 3**. Since electron clouds exist between two borons, fluoride anion is easily overlapped with LUMO of **1**.
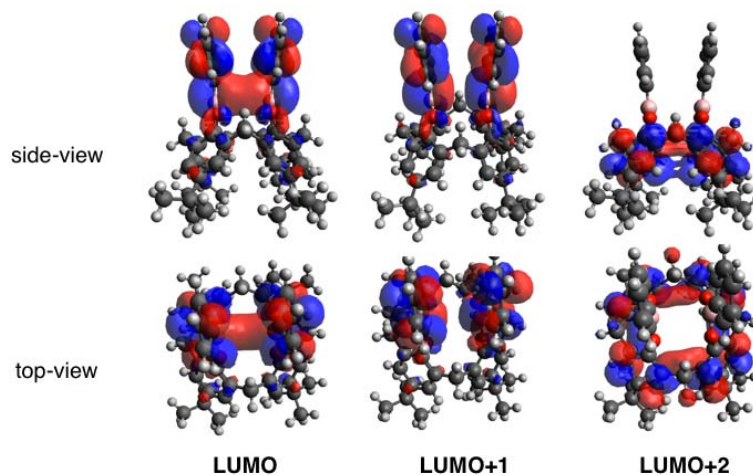

Figure 3. Side and top view of the calculated LUMOs of **1**

NMR Calculation 1

To verify the validity of our calculations, we have been computed H-NMR spectrum of **1**. The **Figure 4** shows the result of calculation at MPW91PW91/6-31+G level. To compare the obtained spectrum with the experimental NMR spectrum of **1**,[9] we conclude that this structure is quite similar to experimental structure.
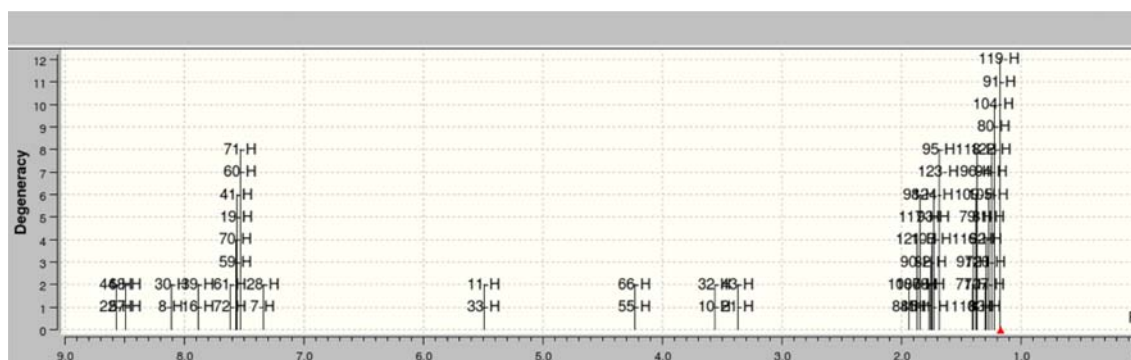

Figure 4. Calculated NMR spectrum of **1** at MPW91PW91/6-31+G level

Geometry Optimization with Fluoride

In general, fluoride combines with its receptor in calix-system with respect to 1:1 or 2:1 ratio. For some cases, main driving force of binding is considered as hydrogen bonding or lewis acid-base mechanism.[10] Furthermore, structures with conical formation of benzene rings also observed because of π-π stacking.[11] Therefore, to optimize the structure with a fluoride ion, we set three models followed by **Figure 5.**
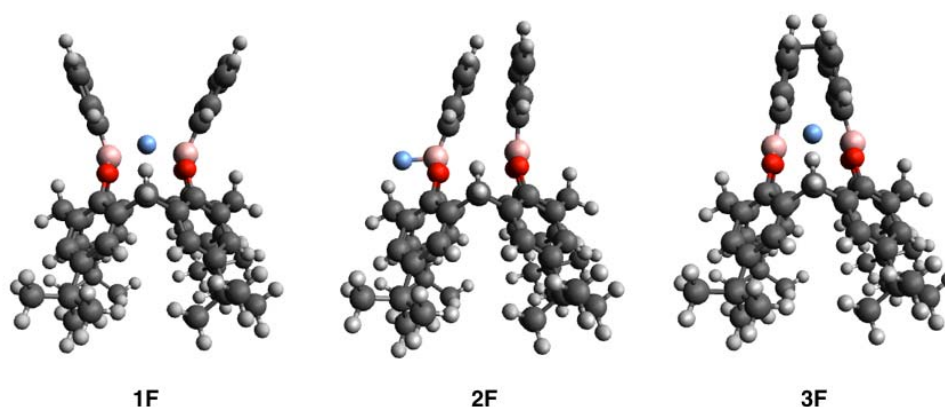

Figure 5. Three suggested model for **1**-Fluoride anion binding structure

By optimizing with same ONIOM level, we obtained optimized **1F** and **2F** structures but the **3F** structure was not converged. Since stacked benzene structures **3** was reported at the system with hydrogen bond,[11] we conclude that the absent of hydrogen bonding in **3F** hinders it to stabilize.

The optimized structure of **2F** indicates that though it reacts with only one side of boron, the π-π stacking effect facilitates **2F** to be stabilized. Such structure of benzene rings in parallel contradicts experimental prediction.[8]
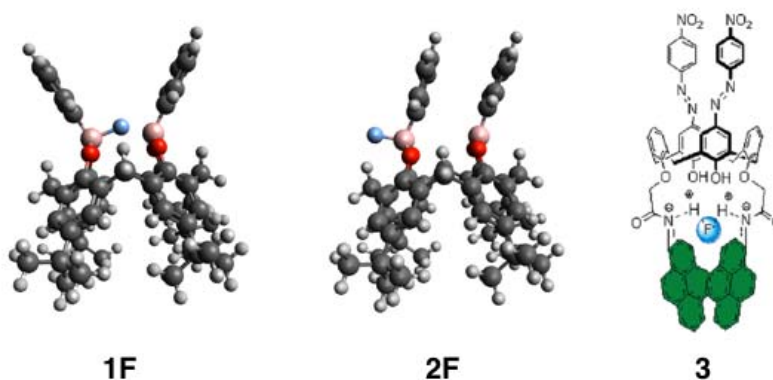

Figure 6. Optimized Structures : 1F, 2F / Calix-system which has hydrogen bonding : 3

NMR Calculation 2

To analyze electronic differences from interaction with fluoride ion, we calculated NMR signal for **1F** moiety at MPW91PW91/6-31+G level. The **Figure 7** shows the result of calculation. By comparing it to the calculated NMR spectrum of **1,** few significant chemical shifts were observed.
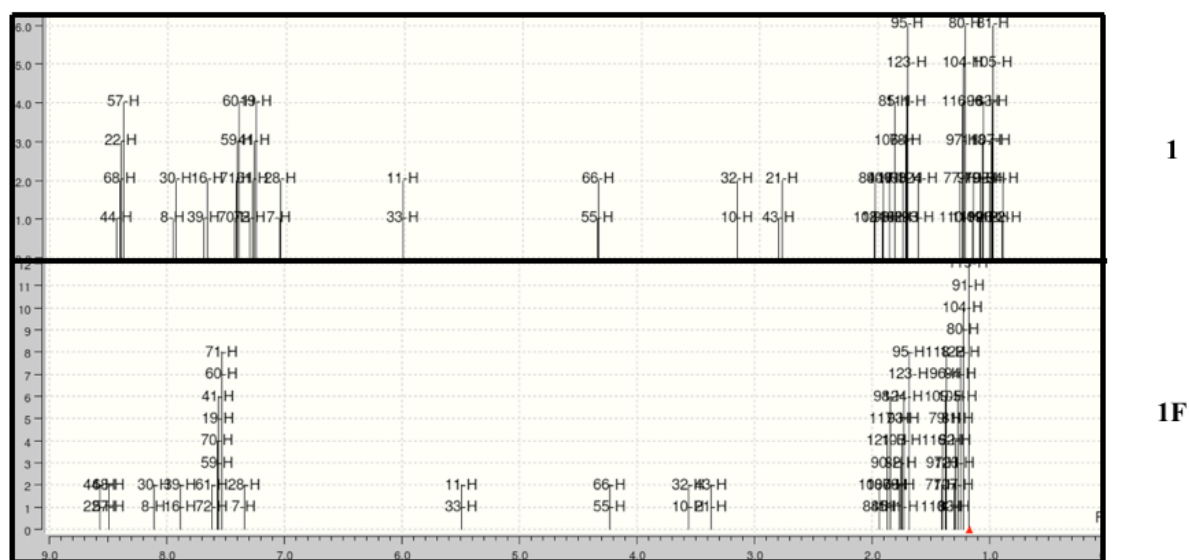

Figure 7. Calculated H-NMR spectrum of **1** and **1F** at MPW91PW91/6-31+G level

The NMR spectrum of 1F shows dramatic proton shifts than non-binding model. These significant shifts occur in the main chain of calixarene. The reduced chain structures are depicted in **Figure 8**.
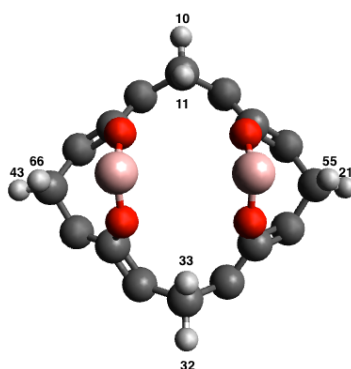

Figure 8. Reduced cyclohexadecane chain of **1F**, labeling for hydrogens

An interesting shift pattern was observed by upfield shift of 11-33H by $\Delta\delta$=-0.5ppm. This pattern can be explained by location of fluoride anion since it binds between two boron atoms. By binding with fluoride anion, its local electric density will be increased. Therefore, it is plausible to say that it is shifted

upward. Also, 66-55H will be not affected by this effect because the bridging boron-oxygen moiety hinders it from fluoride anion. The effect of increasing local density by fluoride will be confined on nearest hydrogen since coulomb interaction decreases rapidly by distance.   Therefore, the 10-32 hydrogen shifts very slightly.

At last, slightly downfield shift $\Delta\delta$=0.6ppm was observed at 21, 43 hydrogens, and it can be explained by LUMO of **1**. For other hydrogens, deshielding was observed at 32-21H and 28-7H by $\Delta\delta$=0.6ppm.

Binding energies for different environments

To obtain a binding energy between the **1** and fluoride anion, we calculated single point energy of each compounds at B3LYP/6-31+G level. The calculated result indicates that its binding energy is about 28.05 kJ/mol. It corresponds with observation that fluoride anion combines with **1** at chloroform solution.

For other halogens, chlorine and bromine, we optimized structures of **1Cl** and **1Br**. We found that the large size of chlorine and bromine anion makes **1Cl** and **1Br** more destabilized, resulting in no binding.
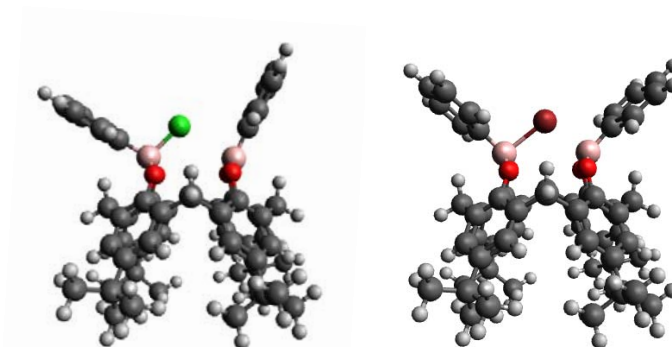

Figure 9. Optimized structure of **1Cl** (left) and **1Br** (right)

To figure out the effect of difference between solvents, we conducted calculation in the acetonitrile as a solvent. Surprisingly, we concluded that the binding between two borons is not possible. However, in this case, the *exo* mechanism can possibly happen with the binding energy as 3.71kJ/mol.
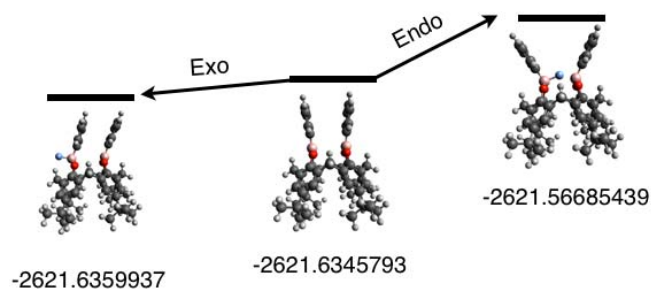
Figure 10. Calculated energies for each system, **1+F-, 1F (*exo), 1F (*endo)** in acetonitrile.

Details of the calculation are followed by **Table 2**.

Energy	F-	1	1+F	1F	Binding energy
Acetonitrile	-99.9920322	-2521.643	-2621.635	-2621.567	-0.06775
Chloroform	-99.9667529	-2521.637	-2621.604	-2621.615	0.01068

Table 2. Calculated binding energies for different systems

Sensing Principles : UV-VIS spectrum and orbital calculation

For **1** and **1F** in the chloroform, results of the UV-visible spectrum calculation with TD-B3LYP are followed by **Figure 11**.
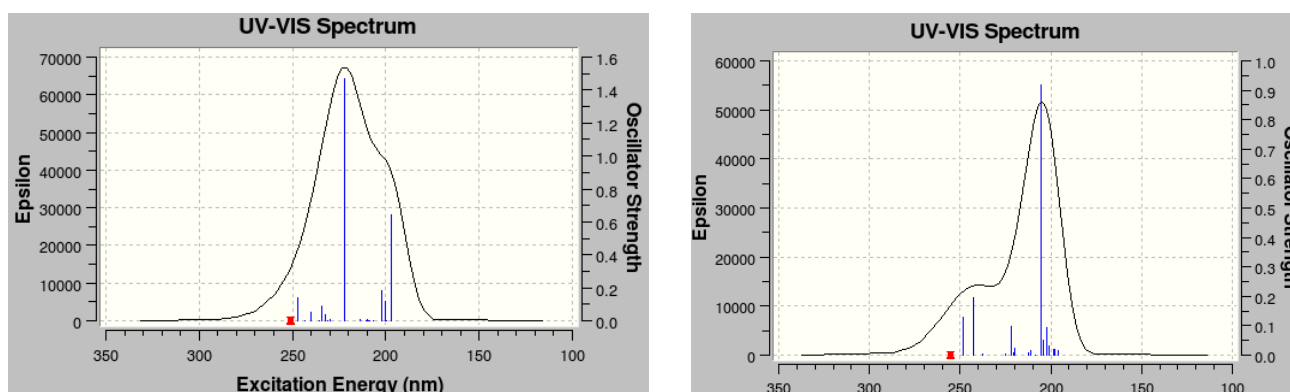

Figure 11. UV-VIS spectrum of **1** (left), **1F** (right)

Comparing the signal **1** with **1F**, we conclude that the binding with fluoride induces colorimetric changes in UV-VIS spectrum. Adding fluoride ion to **1** makes signal weaker, especially at 250nm.

Further, HOMO-LUMO energy level determination in the gas phase and chloroform suggests reason for changes in spectrum pattern. Although formation of complex raises the HOMO and LUMO energy, reduces the difference between HOMO and LUMO. The result of comparing the energy levels in gas phase and chloroform is depicted in **Figure 12.** Considering solvation effect, it doesn't affect on HOMO energy of each state but the polarity of solvent stabilizes LUMO of **1F**. Hence the energy gap between HOMO and LUMO in chloroform reduces greater than in the gas phase, resulting in the fluorescent response.
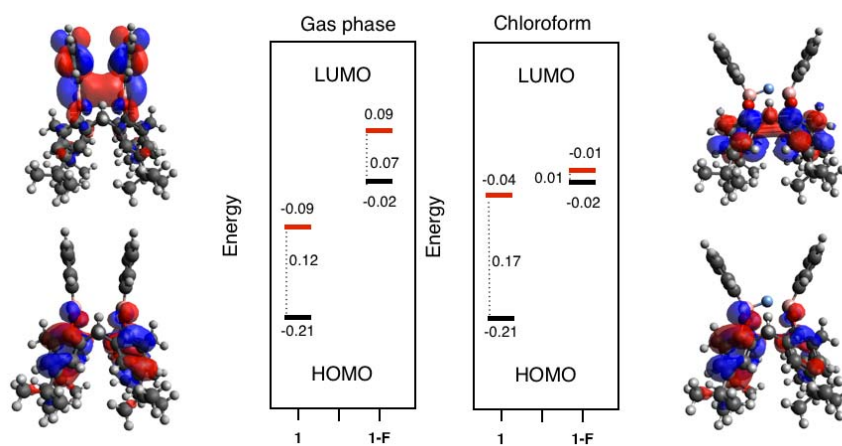

Figure 12. HOMO-LUMO diagrams and energy levels for **1** and **1F-** in both gas phase and chloroform

Conclusion

In conclusion, our calculated results for both the fluoride anion-receptor interaction and the nature of colorimetric and signaling mechanism for 1 are in a good agreement with the reported experimental observations. The optimized structure of 1F shows *endo*-site product for the reaction with fluoride, which shows fluorescent via UV-visible spectroscopy. This pattern was also understood by analyzing molecular orbital level. The energy difference between HOMO and LUMO was reduced by binding with fluoride, resulting in colorimetric sensing. By analyzing NMR signals of 1F, local electron density within reaction site was predicted.

Finally, by calculating single point energy for each receptors at different phases, we found that this host-

guest interaction cannot occurred in gas phase because of destabilized calixarene structure. However, for the case of special solvents, partially stabilized anion helps to interact with receptor to observe colorimetric signals.

References

1. Jooyeon Hong, Sihyun Ham, *Tetrahedron Lett.,* **2008**, *49,* 2393-2396

2. Alba T. Macias, Joseph E. Norton, Jeffrey D. Evanseck, *J. Am. Chem. Soc.,***2003,** *125,* 2351-2360

3. Wendy I. Cross, Matthew P. Lightfoot, *et al.,*   *Inorg. Chem.,* **2000**, *39,* 2690

4. Cho, E. J., Moon. J. W., Ko. S. W., Lee. J. Y., Kim. S. K., Yoon. J., Nam. K. C. *J. Am. Chem. Soc.* **2003**, *125,* 12376

5. Sihuyn Ham, *Bull. Korean. Chem. Soc.,* **2004**, *25*, 1911

6. Melaimi M, Sole S, Chiu C-W, Wang H, Gabbai FP, *Inorg. Chem* **2006**, *45,* 8136-8143

7. Boys, S. F, L Bernardi, F. *Mol. Phys,* **1970**, *19,* 553

8. G. Bifulco, L. Gomez-Paloma, *et al.*, *Org. Lett.*, **2005**, *7 (26),* 5757-5760

9. S. Arimori, M. G. Davidson, *et al., Chem. Commun.*, **2004**, 1640–1641

10. Yun-Dong Wu, Di-Fei Wang, Jonathan L. Sessler, *J. Org. Chem.,* **2001**, *66*, 3739-3746

11. H. J. Kim, S. K. Kim, J. Y. Lee, J. S. Kim, *J. Org. Chem.,* **2006**, *71*, 6611-6614