Theor Chem Acc (2011) 130:1055–1059
DOI 10.1007/s00214-011-1053-2

REGULAR ARTICLE

Role of CH–π interaction energy in self-assembled gear-shaped amphiphile molecules: correlated ab initio molecular orbital and density functional theory study

Jun Koseki · Yukiumi Kita · Shuichi Hiraoka · Umpei Nagashima · Masanori Tachikawa

Received: 21 May 2011 / Accepted: 19 September 2011 / Published online: 8 October 2011

Abstract Ab initio molecular orbital and density functional theory calculations with inclusion of dispersion interaction effect are employed to reveal the characteristic features of intermolecular interactions for the molecular capsule ($\mathbf{1}_6$) consisting of six gear-shaped amphiphile molecules (**1**) discovered by Hiraoka et al. (J Am Chem Soc 130:14368–14369, 2008). The contributions of CH–π and π–π type dispersion energies are found to be indispensable for the formation of hexameric capsule $\mathbf{1}_6$ by the analysis of decomposed interaction energies between fragmented-model species in the **1** molecule. We have also calculated the hexameric capsule ($\mathbf{2}_6$) from demethylated **1** molecule (**2**). Such subtle structural difference induces the different characters of intermolecular interactions, in which the stabilization energy of hexameric $\mathbf{2}_6$ capsule is about 40 kcal/mol smaller than that of the original $\mathbf{1}_6$ capsule, due to the lack of three methyl groups for the CH–π interactions in **2** molecules.

Keywords Gear-shaped amphiphile molecule · Hexameric nano-capsule · Van der Waals force · π–π and CH–π dispersion interaction energies

1 Introduction

Since self-assembled hollow nanostructures have a great potential for being highly functional in the wide area of chemistry, pharmacy, and their interdisciplinary fields, the new types of nano-capsules [1–17] have attracted attention. Recently, Hiraoka et al. [15–17] discovered the gear-shaped molecule (**1**) as shown in Fig. 1a. They reported that the molecules form self-assembled octahedron-shaped metallo-capsules $[\mathrm{M}_6\mathbf{1}_8]^{12+}$, with a series of divalent transition-metal ions, M^{2+} (M = Mn, Fe, Co, Ni, Pd, Pt, Cu, Zn, Cd, and Hg). They also found that the six gear-shaped molecules can form a hexameric capsule $\mathbf{1}_6$ (Fig. 1c) in aqueous methanol without any transition-metal ions by solvophobic effect, while the demethylated gear-shaped molecules (**2**) form no hexameric capsule but a multilayered structure in solid state [18, 19]. The structural difference between these gear-shaped molecules, **1** and **2**, is the existence of only three methyl groups on benzene rings in Fig. 1a, b. The thermodynamic property of the aggregation of **1** was analyzed by isothermal titration calorimetry (ITC) experiment, indicating that the formation of the hexameric capsule $\mathbf{1}_6$ is enthalpically favored but entropically unfavorable [19]. These results suggest that the hexameric capsule $\mathbf{1}_6$ is stabilized by an enthalpic factor arising from van der Waals forces (π–π and CH–π interactions, respectively) between **1**s, while the force between **2**s is smaller due to the lack of three methyl groups in **2**. As these experimental findings emphasize that subtle structural difference of gear-shaped amphiphiles

---

Dedicated to Professor Akira Imamura on the occasion of his 77th birthday and published as part of the Imamura Festschrift Issue.

J. Koseki · Y. Kita · M. Tachikawa (✉)
Quantum Chemistry Division, Graduate School of Science,
Yokohama City University, Kanagawa 236-0027, Japan
e-mail: tachi@yokohama-cu.ac.jp

S. Hiraoka
Department of Basic Science, Graduate School of Arts and
Sciences, The University of Tokyo, Tokyo 153-8902, Japan

U. Nagashima
Research Institute for Computational Science,
National Institute of Advanced Industrial Science
and Technology, Ibaraki 305-8568, Japan

should affect the aggregation property, it is strongly expected that an understanding of hydrophobic surface interaction between molecules in the hexameric capsule guides the future molecular design of novel amphiphiles. Since it is, however, difficult to elucidate the details of such interactions only by experimental approaches, theoretical investigations are indispensable toward the understanding of hydrophobic interaction and to reveal the role of van der Waals interactions between **1** molecules or between **2** ones for the formation of the hexameric capsule.

In this paper, we have performed ab initio molecular orbital (MO) and density functional theory (DFT) calculations including the contribution of dispersion interaction to reveal the characteristic features of intermolecular interactions of the six gear-shaped amphiphile molecules **1**. The computational detail in analyzing intermolecular interactions with some fragment-models is shown in the next section. The results about the role of π–π and CH–π interaction energies in hexameric capsules, $\mathbf{1}_6$ and $\mathbf{2}_6$, are discussed in Sect. 3. Finally, some concluding remarks are given in Sect. 4.

2 Computational detail

To calculate the stabilization energy of hexameric capsule $\mathbf{1}_6$ consisting of six gear-shaped amphiphile molecules **1** in Fig. 1, one has to calculate the energy difference $\Delta E(\mathbf{1}_6) = 6E(\mathbf{1}) - E(\mathbf{1}_6)$ directly, where $E(\mathbf{X})$ is the energy of species **X**. Such direct calculation of the complete hexameric capsule $\mathbf{1}_6$ is, however, much time-consuming and unrealistic with our current computer facilities. Thus, we have used the three fragmented-model species of A, B, and C, which have the same geometry as a part of gear-shaped amphiphile molecule **1** shown in Fig. 2. Checking two-body interactions in hexameric capsule $\mathbf{1}_6$ carefully, we have confirmed that the stabilization energies $\Delta E(\mathbf{1}_6)$ can be approximately estimated from the two-body interaction energies between the two fragmented-model species of AC and BC as,

$$\Delta E(\mathbf{1}_6) = 6 \cdot (\Delta E_{\mathrm{AC}} + \Delta E_{\mathrm{BC}}), \tag{1}$$

where $\Delta E_{\mathrm{AC}} = (E(\mathrm{A}) + E(\mathrm{C})) - E(\mathrm{AC})$ and $\Delta E_{\mathrm{BC}} = (E(\mathrm{B}) + E(\mathrm{C})) - E(\mathrm{BC})$.

In order to analyze the characteristic feature of inter-fragmented-molecular interaction energies such as π–π and CH–π in detail, we have also divided the fragmented-models A, B, and C into smaller fragmented-molecules of D and E species as shown in Fig. 2. The schematic illustrations of the intermolecular interaction between A and C (upper figure) and between B and C (lower figure) are shown in Fig. 3, where the fragmented-pair AC has one π–π and three CH–π interactions, denoted as π–π1, CH–π1, CH–π2, and CH–π3, respectively, while the fragmented-pair BC has similar interactions, denoted as π–π2, CH–π4, CH–π5, and CH–π6, respectively. Thus, the ΔE_{AC} and ΔE_{BC} can be approximately decomposed into

$$\begin{aligned}\Delta E_{\mathrm{AC}} &= \Delta E_{\pi-\pi1} + \Delta E_{\mathrm{CH}-\pi1} + \Delta E_{\mathrm{CH}-\pi2} + \Delta E_{\mathrm{CH}-\pi3},\\ \Delta E_{\mathrm{BC}} &= \Delta E_{\pi-\pi2} + \Delta E_{\mathrm{CH}-\pi4} + \Delta E_{\mathrm{CH}-\pi5} + \Delta E_{\mathrm{CH}-\pi6},\end{aligned} \tag{2}$$

where, for example, the $\Delta E_{\pi-\pi1}$ means the interaction energy of π–π1 as shown in Fig. 3. We note here that the three-body interaction terms such as triple π stacking interactions have been ignored.

We have also calculated the stabilization energy of hexameric capsule $\mathbf{2}_6$ using a similar strategy. We have used the three fragmented-models of A′, B′, and C′, which have the same geometry of a part of gear-shaped amphiphile molecule **2** as shown in Fig. 2.

All the interaction energies between the fragmented-molecules were calculated with the Hartree–Fock (HF) method, 2nd-order Møllor-Plesset perturbation method (MP2), and density functional theory (DFT) with B3LYP and M06 functionals. The 6-31G** basis set was employed in all calculations. Note that the effect of dispersion interaction can be included in the MP2 and DFT with M06 functional calculations. Since there is no X-ray structure for $\mathbf{2}_6$, the positions of all heavy atoms and molecular orientations of each fragmented-molecule were fixed in the geometry of X-ray crystal structure of $\mathbf{1}_6$, while the positions of hydrogen atoms were optimized with HF/6-31G** level. The same molecular geometries and orientations were also employed for

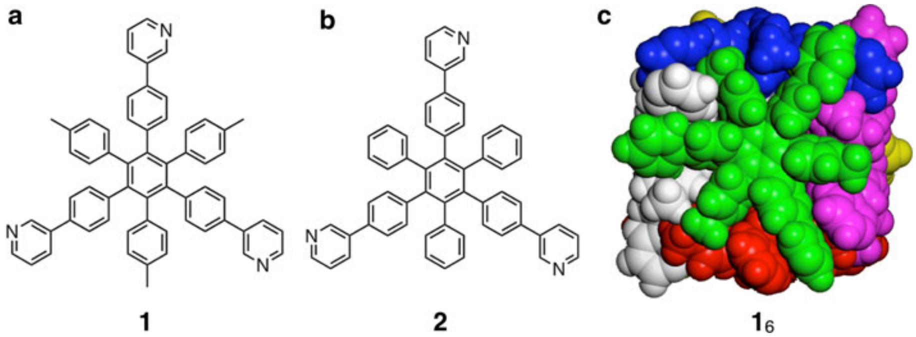

Fig. 1 Chemical structures of **a** methylated and **b** demethylated gear-shaped amphiphile molecules. **c** The crystal structure of a hexameric capsule $\mathbf{1}_6$ with space-filling models is also shown

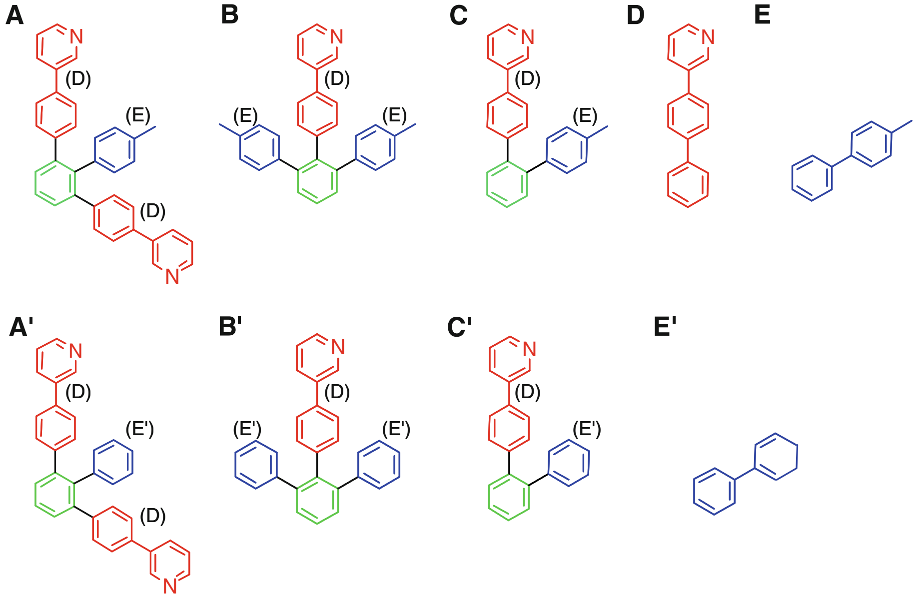

Fig. 2 Fragmented-model structures for gear-shaped molecules. The **A**, **B**, **C**, **D**, and **E** are the models for methylated **1**, and the **A′**, **B′**, **C′**, and **E′** are for demethylated **2**

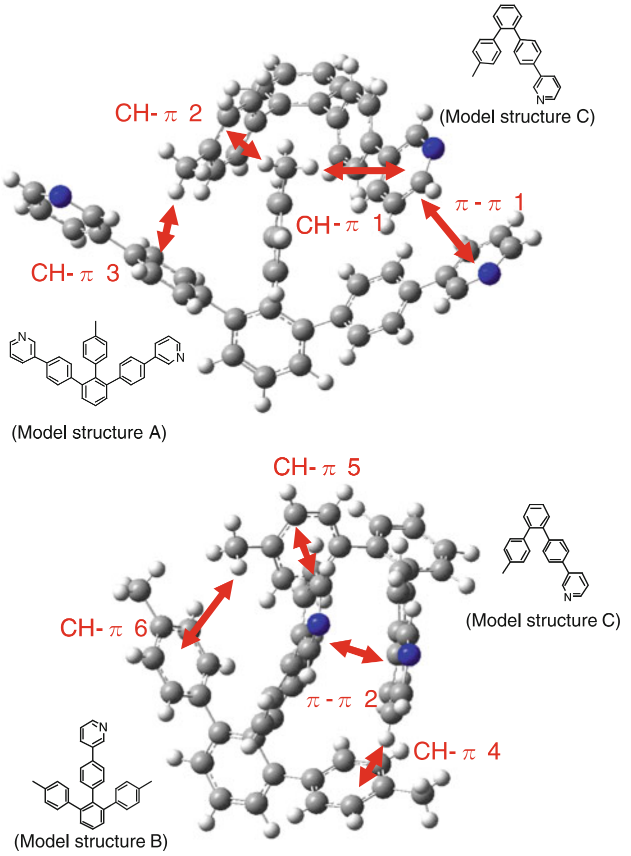

Fig. 3 Intermolecular interactions between *A* and *C* (*upper*), and *B* and *C* (*lower*). The fragment-pair *AC* (*BC*) has a π–π interaction denoted as π–π1 (π–π2), and three CH–π interactions denoted as CH–π1, CH–π2, and CH–π3 (CH–π4, CH–π5, and CH–π6)

calculating the stabilization energy of $\mathbf{2}_6$ in order to analyze the difference of π–π and CH–π interactions between $\mathbf{1}_6$ and $\mathbf{2}_6$. All ab initio molecular orbital calculations were performed with Gaussian 03 and 09 program packages [20, 21].

3 Results and Discussion

Table 1 shows the inter-fragmented-molecular interaction energies of ΔE_{AC} and ΔE_{BC} with HF, MP2, B3LYP, and M06 calculations using 6-31G** basis set. The interaction energies of ΔE_{AC} and ΔE_{BC} with MP2 calculations are 22.2 and 21.3 kcal/mol, respectively, while the HF calculations give the negative values of −5.0 and −2.6 kcal/mol, respectively. Using Eq. (1), the stabilization energy of the complete hexameric capsule $\mathbf{1}_6$ is estimated as $\Delta E(\mathbf{1}_6) = 263\ (-46)$ kcal/mol with the MP2 (HF) method. The DFT calculations give a similar result, that is, the stabilization energy $\Delta E(\mathbf{1}_6)$ of 244 and −25 kcal/mol with M06 and B3LYP functionals, respectively. These results clearly show that the dispersion interactions are indispensable for the formation of hexameric capsules, because the contribution of dispersion force is not included in the calculation of HF and DFT with B3LYP functional calculations while the effect of dispersion interaction can be included in the MP2 and DFT with M06 functional calculations. Table 1 also shows the inter-fragmented-molecular interaction energies of $\Delta E_{\pi-\pi}$ and $\Delta E_{\mathrm{CH}-\pi}$. The interaction energies of ΔE_{AC} and ΔE_{BC} estimated from Eq. (2) are 22.8 (16.7) and 22.3 (15.6) kcal/mol, respectively, which are in reasonable agreement with the corresponding interaction energies of 22.2 (18.3) and 21.3 (15.9) kcal/mol of the original fragmented-molecular pairs with MP2 (DFT with M06 functional). This consistency indicates that the intermolecular interactions of ΔE_{AC} and ΔE_{BC} can be decomposed into the two-body interactions

Table 1 Intermolecular interaction energies of fragmented-molecular pairs AC and BC with HF, MP2, B3LYP, and M06 levels of calculations using 6-31G** basis set

The energies decomposed into the smaller fragmented-molecules of D and E are also shown. All units in kcal/mol

	ΔE_{AC}	$\Delta E_{\pi-\pi 1}$	$\Delta E_{\mathrm{CH}-\pi 1}$	$\Delta E_{\mathrm{CH}-\pi 2}$	$\Delta E_{\mathrm{CH}-\pi 3}$
HF	−5.0	−0.2	−1.5	−2.5	−2.5
MP2	22.2	6.8	6.6	5.2	4.2
B3LYP	−2.0	0.2	−0.5	−1.2	−1.1
M06	18.3	4.6	4.9	4.4	2.8
	ΔE_{BC}	$\Delta E_{\pi-\pi 2}$	$\Delta E_{\mathrm{CH}-\pi 4}$	$\Delta E_{\mathrm{CH}-\pi 5}$	$\Delta E_{\mathrm{CH}-\pi 6}$
HF	−2.6	−2.5	−0.1	0.3	−0.2
MP2	21.3	9.7	4.7	4.8	3.1
B3LYP	−0.6	−1.5	0.5	0.6	0.2
M06	15.9	6.6	3.2	3.41	2.4

Table 2 Intermolecular interaction energies of fragmented-molecular pairs A′C′ and B′C′ with HF, MP2, B3LYP, and M06 levels of calculations using 6-31G** basis set

The energies decomposed into the smaller fragmented-molecules of D′ and E′ are also shown. All units in kcal/mol

	$\Delta E_{\mathrm{A}'\mathrm{C}'}$	$\Delta E_{\pi-\pi 1}{}'$	$\Delta E_{\mathrm{CH}-\pi 1}{}'$	$\Delta E_{\mathrm{CH}-\pi 2}{}'$	$\Delta E_{\mathrm{CH}-\pi 3}{}'$
HF	−3.8	−0.2	−1.1	−2.3	−0.8
MP2	16.9	6.8	5.0	3.0	2.7
B3LYP	−1.4	0.2	−0.3	−1.3	−0.2
M06	12.4	4.6	3.4	2.0	1.2
	$\Delta E_{\mathrm{B}'\mathrm{C}'}$	$\Delta E_{\pi-\pi 2}{}'$	$\Delta E_{\mathrm{CH}-\pi 4}{}'$	$\Delta E_{\mathrm{CH}-\pi 5}{}'$	$\Delta E_{\mathrm{CH}-\pi 6}{}'$
HF	−1.7	−2.5	0.10	0.6	0.3
MP2	19.3	9.7	4.1	4.4	2.1
B3LYP	0.1	−1.5	0.6	0.8	0.5
M06	13.4	6.6	2.4	2.8	1.2

between smaller fragmented-molecules, and the three-body interaction can be ignored.

Tables 2 shows the inter-fragmented-molecular interaction energies of $\Delta E_{\mathrm{A}'\mathrm{C}'}$ and $\Delta E_{\mathrm{B}'\mathrm{C}'}$ with HF, MP2, B3LYP, and M06 calculations using 6-31G** basis set. The $\Delta E_{\mathrm{A}'\mathrm{C}'}$ and $\Delta E_{\mathrm{B}'\mathrm{C}'}$ with MP2 (DFT with M06 functional) calculations are 16.9 (12.4) and 19.3 (13.7) kcal/mol, respectively, while the HF (DFT with B3LYP functional) calculations give the negative values of −3.8 (−1.4) and −1.7 (0.1) kcal/mol, respectively. From the MP2 (DFT with M06 functional) calculation, the stabilization energy of whole hexameric capsule $\mathbf{2}_6$ is estimated as $\Delta E(\mathbf{2}_6) = 219$ (195.4) kcal/mol. We address here that the stabilization energies of $\mathbf{2}_6$ are about 40 and 50 kcal/mol smaller than that of $\mathbf{1}_6$ in the MP2 and DFT with M06 functional levels, respectively. Table 2 also shows the intermolecular interaction energies between the smaller fragmented-molecules. The interaction energies of $\Delta E_{\mathrm{A}'\mathrm{C}'}$ and $\Delta E_{\mathrm{B}'\mathrm{C}'}$ estimated from Eq. (2) are the values 17.5 (11.2) and 20.3 (12.9) kcal/mol, respectively, which are indeed close to the corresponding energies of 16.9 (12.4) and 19.3 (13.7) kcal/mol for the original fragmented-molecular-pairs with MP2 (DFT with M06 functional) results. This result is quite similar in the case of fragmented-pairs AC and BC as shown in Table 1.

To analyze such difference of the stabilization energies of $\mathbf{1}_6$ and $\mathbf{2}_6$ in detail, we would focus on the interaction energies between the smaller fragmented-molecules obtained with the MP2 calculations. Tables 1 and 2 clearly show that all the decomposed CH–π interaction energies of $\Delta E_{\mathrm{CH}-\pi}$ in **1** are greater than those in **2**, while all the decomposed π–π interaction energies, $\Delta E_{\pi-\pi}$, in both **1** and **2** are quite close to each other. This result clearly indicates that the difference of the stabilization energy between $\mathbf{1}_6$ and $\mathbf{2}_6$ arises from the CH–π interaction energies, related to the three methyl groups on **1**.

Experimentally, the methylated gear-shaped molecules (**1**) are able to form hexameric capsules $\mathbf{1}_6$ in aqueous methanol while demethylated gear-shaped molecules (**2**) are unable [18, 19]. Our static ab initio MO and DFT results of the intermolecular interactions indicate the possibility of the formation of the hexameric capsule of **2** molecules, although the stabilization energy of $\mathbf{2}_6$ is about 40 (or 50) kcal/mol smaller than that of $\mathbf{1}_6$. We consider that the dynamical feature of the corresponding thermal fluctuation should be related to the reason why the molecule **2** cannot form hexameric capsules experimentally. A molecular dynamics simulation at finite temperature will be required for such analysis. The solvation effect is also an interesting subject. Such theoretical simulations are now in progress in our group.

4 Conclusions

We have applied ab initio molecular orbital and density functional theory calculations with inclusion of dispersion interaction effect to the gear-shaped amphiphile molecule (**1**) and demethylated **1** molecule (**2**) in order to reveal the role of van der Waals forces of π–π and CH–π interactions in forming the hexameric capsule. Using the fragmented-models for **1** and **2** molecules, we have found that the stabilization energy of hexameric capsule $\mathbf{1}_6$ and $\mathbf{2}_6$ is 263 and 219 kcal/mol in MP2 level of calculation, respectively, although the HF calculations give the negative value of -46 and -34 kcal/mol, respectively. The DFT calculations with M06 functional also give the similar results. Our theoretical results strongly support that the gear-shaped amphiphile molecules can be aggregated by van der Waals dispersion forces. We have also found that all CH–π interactions in the molecular capsule $\mathbf{1}_6$ are greater than those in the capsule $\mathbf{2}_6$ due to the lack of three methyl groups in **2** molecules.

Acknowledgments We would like to acknowledge Grant-in-Aid for Scientific Research and for the priority area by Ministry of Education, Culture, Sports, Science and Technology, Japan.

References

1. Rebek J Jr (2005) Angew Chem Int Ed 44:2068–2074
2. Lützen A (2005) Angew Chem Int Ed 44:1000–1002
3. Kobayashi K, Shirasak T, Yamaguchi K, Sakamoto S, Horn E, Furukawa N (2000) Chem Commun 41–42
4. Purse BW, Rebek J Jr (2005) Proc Natl Acad Sci USA 102:10777–10782
5. Shimizu S, Kiuchi T, Pan N (2007) Angew Chem Int Ed 46:6442–6445
6. Baillargeon P, Dory YL (2008) J Am Chem Soc 130:5640–5641
7. Dalgarno SJ, Power NP, Atwood JL (2008) Coord Chem Rev 252:825–841
8. Fiedler D, Bergman RG, Raymond KN (2004) Angew Chem Int Ed 43:6748–6758
9. Pluth MD, Bergman RG, Raymond KN (2007) Science 316:85–88
10. Yoshizawa M, Tamura M, Fujita M (2006) Science 312:251–254
11. Sato S, Iida J, Suzuki K, Kawano M, Ozeki T, Fujita M (2006) Science 313:1273–1276
12. Yamanaka M, Yamada Y, Sei Y, Yamaguchi K, Kobayashi K (2006) J Am Chem Soc 128:1531–1539
13. Haino T, Kobayashi M, Fukazawa Y (2006) Eur J Chem 12:3310–3319
14. Ikeda A, Udzu H, Zhong Z, Shinkai S, Sakamoto S, Yamaguchi K (2001) J Am Chem Soc 123:3872–3877
15. Hiraoka S, Harano K, Shiro M, Shionoya M (2005) Angew Chem Int Ed 44:2727–2731
16. Hiraoka S, Harano K, Shiro M, Ozawa Y, Yasuda N, Toriumi K, Shionoya M (2006) Angew Chem Int Ed 45:6488–6491
17. Harano K, Hiraoka S, Shionoya M (2007) J Am Chem Soc 129:5300–5301
18. Hiraoka S, Harano K, Shiro M, Shinoya M (2008) J Am Chem Soc 130:14368–14369
19. Hiraoka S, Harano K, Nakamura T, Shiro M, Shionoya M (2009) Angew Chem Int Ed 48:7006–7009
20. Frisch MJ, Trucks GW, Schlegel HB et al (2004) GAUSSIAN 03. Gaussian, Inc., Wallingford
21. Frisch MJ, Trucks GW, Schlegel HB et al (2009) GAUSSIAN 09. Gaussian, Inc., Wallingford