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〈Research Paper〉

Design and Synthesis of Novel Rhodamine-Based Chemosensor Probe Toward Cu^{2+} Cation

Young-A Son†

BK21, Department of Advanced Organic Materials Engineering, Chungnam National University, Daejeon, Korea

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Abstract: Nowdays, fluorescent rhodamine chemosensors have attracted a worldwide interest due to its ability to selectively detect heavy and transition metal cations. Due to the importance in environmental and biological toxic effects, the developments of fluorescent chemosensors have been received considerable attention in recent. Especially, a rhodamine-based chemosensor probes have been proved to be useful by exhibiting the efficient "off-on" fluorescence switching toward selected metal cations. This fluorophore can undergo the transformation from non-fluorescent and colorless spirolactam derivative to fluorescent ring-open form. In this study, a new fluorescent chemosensor was synthesized using rhodamine B through two-step procedures, and its selectivity and related optical property were characterized. Selectivity and sensitivity was found toward Cu^{2+} guest molecules and then related optical properties of rhodamine B based fluorescent chemosensor compound were characterized using discussed. In addition, computational calculation was used to determine the HOMO/LUMO values.

Keywords: *rhodamine, fluorescence, chemosensor, divalent copper(Cu^{2+}), HOMO/LUMO*

1. Introduction

Heavy metal cations have crucial role in a wide range of chemical and biological processes. Among the transition metal cations, divalent copper (Cu^{2+}) is an essential trace element for many physiological systems and it plays a catalytic cofactor for a variety of transcriptional event[1,2]. Conversely, under overloading concentration, copper exhibits severe toxic problem and can cause neurodegenerative diseases (e.g., Alzheimer's and Wilson's diseases)[3-5].

Thus, there is an urgent need for effective, simple and real-time monitoring system. Abused amounts of copper cause a great prejudicial effect for human health and the environment. In this regard, the design and synthesis of novel chemosensors which can detect heavy metal cations with selectivity and sensitivity were highly worthy. These chemosensors may provide a less labor-consuming and a simple technical alternative to determine hazardous guest molecules.

It could be effectively applied in biological environmental systems[6-8].

Due to the good stability of Schiff base ligands with Cu^{2+} to form complexes, rhodamine Schiff base ligands have been attracted a great attention in recent years[9]. On the basis of well-known ring-closed spirolactam (colorless, non-fluorescent) to ring-opened amide (colored, fluorescent) reaction, rhodamine derivatives have been extensively considered with an ideal model, that have been commonly utilized to prepare fluorophore materials for various metal cations[10-12].

In this context, we have prepared new designed chemosensor probe using rhodamine B hydrazide and indole-3-carboxaldehyde. The obtained sensor showed clear selectivity and sensitivity toward Cu^{2+} with compared to other hazardous metal cations. This finding might be utilized into various monitoring system and platform for environmental demands.

2. Experimental

2.1 Measurement

All the reagents and solvents, used for synthesis of rhodamine B based probe 1, were purchased form Aldrich and used without further purification.

†Corresponding author: Young-A Son (yason@cnu.ac.kr)
Tel.: +82-42-821-6620 Fax.: +82-42-821-8870

Absorption and fluorescence spectra of the prepared novel probe 1 were measured with and Agilent 8453 spectrophotometer and a Shimadzu RF-5301PC fluorescent spectrophotometer, respectively. ^{1}H-NMR spectra were recorded with AVANCE III 600 spectrometer operated at 600MHz NMR. HRMS data was recorded on a JEOL M Station [JMS-700]. HOMO/LUMO calculation and modelling simulation proceed with DMol^3 of *Material Studio 4.3*.

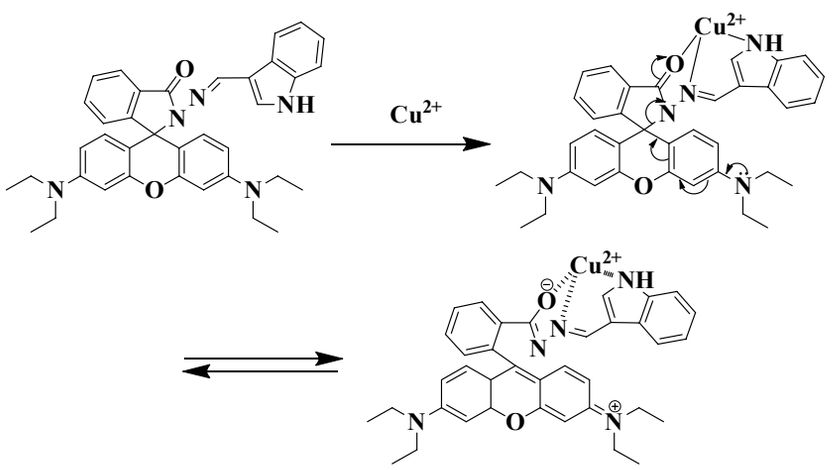
2.2 Design of probe 1

A novel rhodamine probe 1 was synthesized from the reaction of rhodamine B hydrazine, followed by reaction with indol-3-carboxaldehyde for the detection toward Cu^{2+}. For this design concept, complex mechanism of probe 1 for Cu^{2+} was proposed in scheme 1.

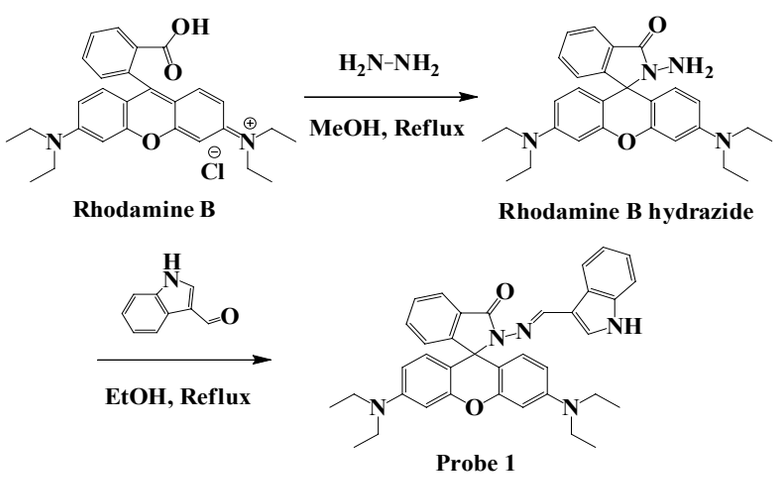
Cu^{2+} was likely bound to N atom of indol-3-carboxaldehyde group as well as another N atom of the Schiff base and O atom of carbonyl group in a spirolactam moiety of rhodamine B. As a result, the spirolactam form of rhodamine B could be broken and consequently the typical pink fluorescence of rhodamine-based chemosensor would be detected[13].

2.3 Synthesis of probe 1

Rhodamine B hydrazide was synthesized according to the literature procedure[14]. Rhodamine B hydrazide (0.46g, 1mmol) was dissolved in 20mL of absolute ethanol. Addition of indole-3-carboxaldehyde (0.17g, 1.2mmol) to the reaction mixture was refluxed for 8h. The solution was then concentrated and allowed to stand at room temperature through overnight.



Scheme 1. The binding reaction of probe 1 with Cu^{2+}



Scheme 2. Synthesis of rhodamine B based probe 1

The precipitate was filtered the following day, washed several times with cold ethanol, recrystallized from MeCN and dried under reduced pressure to afford probe 1 (0.40g) with 68% yield as a light yellow solid (Scheme 2). Mp = 246-249℃. ^{1}H-NMR (600MH_Z, $CDCl_3$, ppm), the following chemical shifts were recorded: 11.48 (1H, s), 9.41 (1H, s), 7.87 (1H, d, *J*=7.153), 7.70 (1H, d, *J*=2,824), 7.68 (1H, s), 7.56-7.62 (2H, m), 7.33 (1H, d, *J*=8.904), 7.16 (1H, d, *J*=7.341), 7.10 (1H, t, *J*=7.341), 6.93 (1H, t, *J*=7.341), 6.44 (2H, d, *J*=2.259), 6.41 (1H, s), 6.39 (1H, s), 6.34 (1H, d, *J*=2.259), 6.32 (1H, d, *J*=2.259), 3.27-3.31 (8H, q, *J*=6.964), 1.05 (12H, t, *J*=6.694). EI$^{(+)}$-HRMS (m/z): $[M+H]^+$ calcd. for $C_{37}H_{37}N_5O_2$: 583.2947, found 583.2917.

3. Result and Discussion

3.1 Selectivity of probe 1

Selectivity of probe 1 toward various metal cations was investigated by UV-Vis spectroscopy in the MeCN solution and the results are shown in Figure 1. In absorption monitoring, however, none of the metal cations showed any discernible spectral absorption with selective point of view. In this regard, selectivity of probe 1 with various metal cations was not satisfactory to be utilized.

Figure 2 explains the fluorescent turn-on response of probe 1 with various metal cations. When 10μM of each metal cations was mixed with probe 1, there were no considerable changes in fluorescent emissions with other metal cations except Cu^{2+} which showed a clear fluorescent emission signal. With the addition of Cu^{2+} to the probe 1, fluorescence intensity of probe 1 displayed a spectacular increase and its wavelength was maximized at 578 nm. These results indicate that probe 1 showed a significant selective function toward Cu^{2+}. In this regard, probe 1 is utilized as an appropriate chemosensor toward Cu^{2+} detection.

To observe selectivity for Cu^{2+} over other metal cations, the affinity competition of probe 1 for various metal cations was investigated. As shown in Figure 3, fluorescent enhancement caused by the mixture of Cu^{2+} with other metal cations was similar to that caused

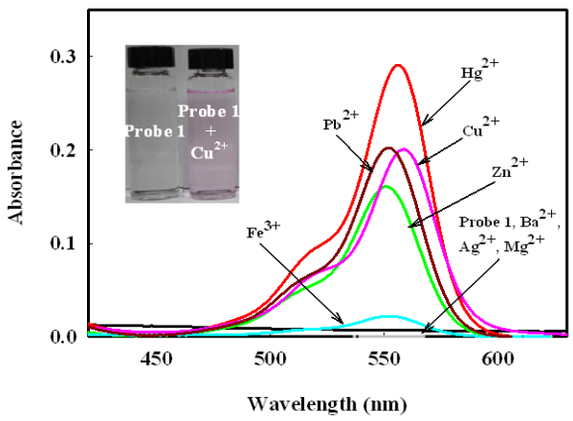


Figure 1. Absorption spectra of probe 1 (10μM) upon the addition of various metal cations (10μM) in MeCN. Inset: the photograph of the color change before and after the addition of Cu^{2+} to a solution of probe 1.

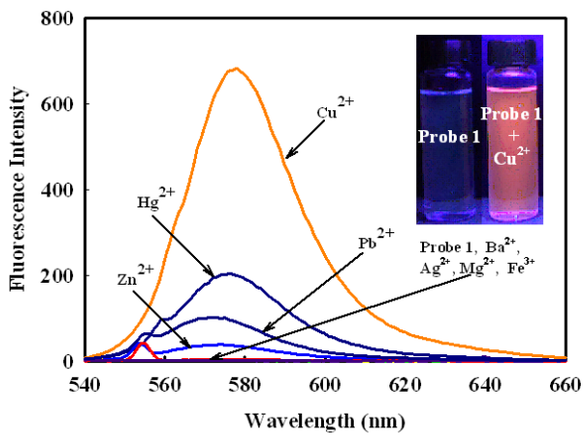


Figure 2. Emission spectra of probe 1 (10μM) upon addition of various metal cations (10μM) in MeCN. Inset: the photograph of the fluorescence change before and after the addition of Cu^{2+} to a solution of probe 1.

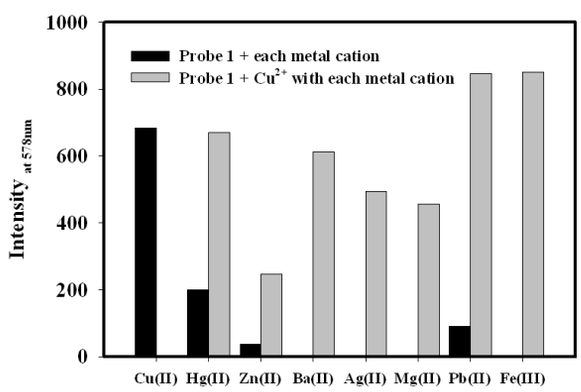


Figure 3. Fluorescence response of probe 1 to Cu^{2+} or to various metal cations (the black bar portion) and to the mixture of other metal cations with Cu^{2+} (the gray bar portion) in MeCN.

by Cu^{2+} only. The result demonstrated that probe 1 has higher binding affinity toward Cu^{2+} than other various metal cations. Thus, this sensor can be used to detect Cu^{2+}, even though any target environmental samples have various metal cations.

3.2 Sensitivity of probe 1

UV-Vis titration absorption spectra of different mole concentrations of Cu^{2+} with probe 1 in MeCN solution is depicted in Figure 4. The probe 1 exhibits extremely weak absorption in the visible range in the absence of Cu^{2+} due to probe 1 exists in the form of the ring-closed spirolactam structure in the solution. However, the addition of Cu^{2+} to the probe 1 solution leads to a dramatic change in the visible range and a distinct new peak at 559 nm was observed. Meanwhile, the colorless solution of probe 1 rapidly turned into pink: suggesting the formation of the ring-opened amide form of probe 1 upon Cu^{2+} binding. In this regard, probe 1 exhibits a significant Cu^{2+}-induced absorption. From inset figure, one can see that the absorption intensity increased with increasing Cu^{2+} concentration up to 10μM and then remained as a constant. This finding indicates the titration curve to be assumed a 1:1 stoichiometry and this binding mode of probe 1-Cu^{2+} complexes was also supported by a Job's plot[15].

For the measurement of Job's plot method, various molar ratios between probe 1 and Cu^{2+} (1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, 9:1, 10:0) in MeCN were prepared. Total concentration of probe 1+Cu^{2+} complex was kept at 100μM. The relationship between maximum absorption peaks versus different mole fractions is shown in Figure 5. Maximum absorption peak was reached when the molar fraction was 0.5. In this regard, these results indicate a 1:1 ratio for probe 1-Cu^{2+} complex, in which Cu^{2+} was bound with a probe 1. And this behaviour provides a good opportunity to detect Cu^{2+} with high sensitivity.

With further investigations, Figure 6 shows a variation of fluorescent spectra as a function of Cu^{2+} concentration which was measured to evaluate its sensing behaviour by means of fluorescent titration in MeCN.

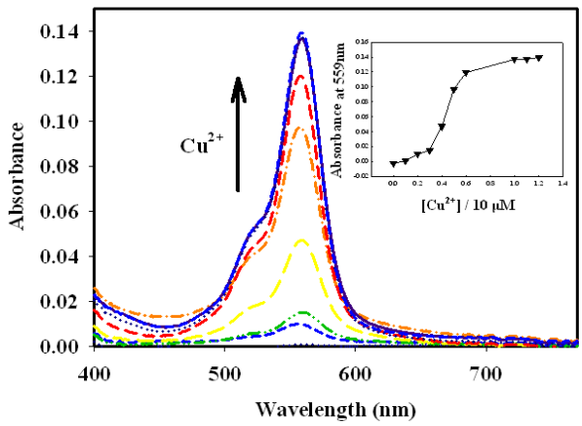


Figure 4. Absorption spectra of probe 1 (10μM) with addition increasing concentration (0~1.4equiv.) of Cu^{2+} in MeCN. Inset: absorbance at 559 nm of probe 1 as a function of Cu^{2+} concentration.

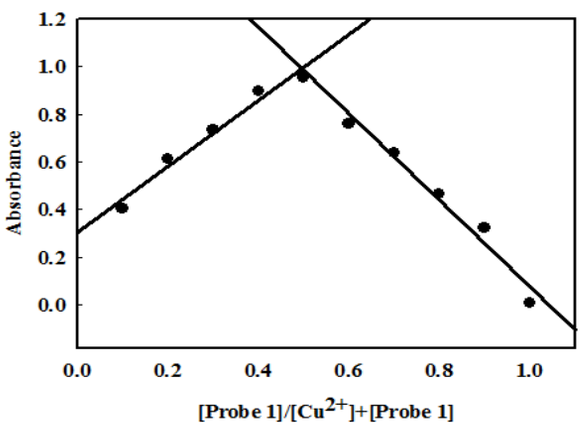


Figure 5. Job's plot analysis of probe 1 with Cu^{2+} in MeCN. Total concentration of probe 1+Cu^{2+} was kept constant at 100μM.

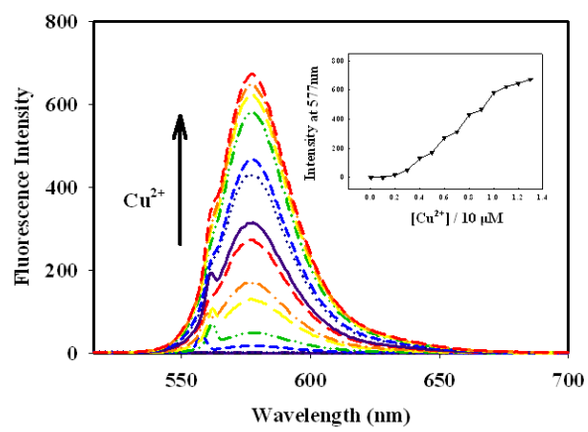


Figure 6. Fluorescence spectra of probe 1 (10μM) with addition increasing concentration (0~1.4equiv.) of Cu^{2+} in MeCN. Inset: emission intensities at 577 nm of probe 1 as a function of Cu^{2+} concentration.

With increasing Cu^{2+} concentration, new emission fluorescent intensity gradually increased at 577 nm. This increase in fluorescent intensity clearly demonstrated that probe 1 can serve as a highly sensitive chemosensor for Cu^{2+} detection.

3.3 Computational simulation of probe 1

We have computationally calculated to investigate electron distributions and HOMO/LUMO energy levels of probe 1. It has been simulated with *Material Studio 4.3 suite* program which is the quantum mechanical code using density functional theory (DFT).

Perdew-Burke-Ernzerhof (PBE) function of generalized gradient approximation (GGA) level with double numeric polarization basis set was used to calculate the energy level of the frontier molecular orbits[16-18].

As shown in Figure 7, electron distributions and its HOMO/LUMO energy levels of probe 1 were calculated. Related HOMO/LUMO values were calculated to be -4.372eV and -2.024eV respectively. In this regard, the △E value was finally calculated to be 2.348eV. Electron density distribution of the molecular skeleton reveals that at HOMO distribution of the probe 1, it was located essentially over the indole-3-carboxaldehyde moiety, while at LUMO state, it was mainly distributed over spirolactam moiety. This indicates that probe 1 has interesting property of intramolecular charge transfer system.

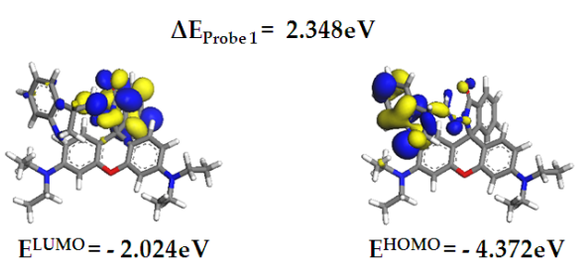


Figure 7. Electron distributions and HOMO/LUMO energy levels of probe 1.

4. Conclusions

In summary, a novel fluorometric probe 1 for Cu^{2+} detection based on the ring-opening of spirolactam was designed and synthesized via the nucleophilic addition reaction of indole-3-carboxaldehyde and rhodamine B hydrazide. Studies showed that probe 1 exhibited highly selective and sensitive to Cu^{2+} with compared to other metal cations such as Hg^{2+}, Pb^{2+}, Mg^{2+}, Zn^{2+}, Ag^{2+}, Ba^{2+} and Fe^{3+}. Binding configuration between probe 1 and Cu^{2+} was elucidated to 1:1 stoichiometry complex, which was determined with Job's plot method. HOMO/LUMO energy potential was calculated and movement of electron density distribution was simulated with computational simulation system.

Acknowledgments

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References

1. A. Sikdar, S. S. Panja, P. Biswas, and S. Roy, A Rhodamine-based dual Chemosensor for Cu(II) and Fe(III), *J. of Fluorescence*, **22**(1), 443(2012).
2. X. Ma, J. Liu, Y. G. Du, G. H. Wei, and D. B. Wei, New Rhodamine Derivative as "off–on" Fluorescent Chemosensor for Detection of Cu^{2+}, *Science China Chemistry*, **54**(10), 1635(2011).
3. C. Yu, J. Zhang, R. Wang, and L. Chen, Highly Sensitive and Selective Colorimetric and "off–on" Fluorescent Probe for Cu^{2+} Based on Rhodamine Derivative, *Organic and Biomolecular Chemistry*, **8**, 5277(2010).
4. S. H. Hahn, M. S. Tanner, D. M. Danke, and W. A. Gahl, Normal Metallothionein Synthesis in Fibroblasts Obtained from Children with Indian Childhood Cirrhosis or Copper-Associated Childhood Cirrhosis, *Biochemical and Molecular Medicine*, **54**(2), 142(1995).
5. K. J. Barnham, C. L. Masters, and A. I. Bush, Neurodegenerative Diseases and Oxidative Stress, *Nature Review Drug Discovery*, **3**, 205(2004).
6. L. Jiang, L. Wang, B. Zhang, G. Yin, and R. Y.

Wang, Cell Compatible Florescent Chemosensor for Hg^{2+} with High Sensitivity and Selectivity Based on the Rhodamine Fluorophore, *European J. of Inorganic Chemistry*, **28**, 4438(2010).

7. F. Yan, D. Cao, N. Yang, Q. Yu, M. Wang, and L. Chen, A Selective "turn–on" Fluorescent Chemosensor Based on Rhodamine for Hg^{2+} and its Application in Live Cell Imaging, *Sensors and Actuators B: Chemical*, **162**(1), 313(2012).
8. Y. K. Yang, K. J. Yook, and J. Tae, A Rhodamine-Based Fluorescent and Colorimetric Chemodosimeter for the Rapid Detection of Hg^{2+} Ions in Aqueous Media, *J. of the American Chemical Society*, **127**(48), 16760(2005).
9. W. Y. Liu, H. Y. Li, H. S. Lv, B. X. Zhao, and J. Y. Miao, A Rhodamine Chromene-based "turn –on" Fluorescence Probe for Selectively Imaging Cu^{2+} in Living Cell, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **95**, 658(2012).
10. A. J. Weerasinghe, C. Schmiesing, S. Varaganti, G. Ramakrishna, and E. Sinn, Single- and Multiphoton Turn-On Fluorescent Fe^{3+} Sensors Based on Bis(rhodamine), *J. of Physical Chemistry B*, **114**, 9413(2010).
11. H. Li, J. Fan, F. Song, H. Zhu, J. Du, S. Sun, and X. Peng, Fluorescent Probes for Pd^{2+} Detection by Allylidene-Hydrazone Ligands with Excellent Selectivity and Large Fluorescence Enhancement, *Chemistry A European J.*, **16**(41), 12349 (2010).
12. X. Chen, T. Pradhan, F. Wang, J. S. Kim, and J. Y. Yoon, Fluorescent Chemosensors Based on Spiroring-Opening of Xanthenes and Related Derivatives, *Chemical Review A*, **112**(3), 1910(2011).
13. Y. Zhao, B. Zheng, J. Du, D. Xiao, and L. Yang, A Fluorescent "turn-on" Probe for the Dual-channel Detection of Hg(II) and Mg(II) and its Application of Imaging in Living Cells, *Talanta*, **85**(4), 2194(2011).
14. X. F. Yang, X. Q. Guo, and Y. B. Zhao, Development of a Novel Rhodamine-type Fluorescent Probe to Determine Peroxynitrite, *Talanta*, **57**(5), 883 (2002).
15. J. Wang and X. Qian, A Series of Polyamide Receptor Based PET Fluorescent Sensor Molecules: Positively Cooperative Hg^{2+} Ion Binding with High Sensitivity, *Organic Letters*, **8**(17), 3721(2006).
16. B. Delley, An All-electron Numerical Method for Solving the Local Density Functional for Polyatomic Molecules, *J. of Chemical Physics*, **92**, 508 (1990).
17. M. Cho, Two-dimensional Vibrational Spectroscopy VII, Investigation of the Vibronic and Vibrational Couplings by using Novel Triply Sesonant Two-dimensional Vibrational Spectroscopies, *J. of Chemical Physics*, **113**, 7746(2000).
18. A. D. Boese and N. C. Handy, A New Parametrization of Exchange-correlation Generalized Gradient Approximation Functionals, *J. of Chemical Physics*, **114**, 5497(2001).