

A new ratiometric and colorimetric chemosensor for cyanide anion based on Coumarin–hemicyanine hybrid†

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A hybrid coumarin–hemicyanine dye, **Cou-BT**, was developed as a new ratiometric and colorimetric sensor for cyanide with a sensing mechanism *via* nucleophilic addition of cyanide anion to the benzothiolium group. **Cou-BT** shows high sensitivity and selectivity for cyanide detection over other common anion species in aqueous acetonitrile solution. The calculated pseudo-first-order rate constant for cyanide anion addition was $(2.13 \pm 0.08) \times 10^{-2} \text{ s}^{-1}$ at 298 K, and the detection limit was estimated to be 0.64 μM . The DFT and TDDFT calculation results suggest that the ratiometric and colorimetric sensing behavior of **Cou-BT** upon its reaction with cyanide was due to the interrupted π -conjugation and blocked ICT progress.

Introduction

Cyanide is a well-known hazardous chemical both in biology and the environment due to its extremely high toxicity to mammals. The cyanide poisoning of mammals can lead to vomiting, loss of consciousness, and finally death.¹ According to the World Health Organization, the maximum acceptable level of cyanide in drinking water is 1.9 μM .² Moreover, the widespread use of cyanide in petrochemical, gold mining, photographic, and steel manufacturing have caused a serious environmental concern.¹ Thus, there is considerable interest in the development of effective detection methods of high selectivity and sensitivity for cyanide anion, especially in water and physiological conditions.

Recently, fluorescent sensors for cyanide anion have received great attention owing to their simple, selective, and rapid implementation.³ Several strategies, such as the coordination of cyanide anions with metal ion/boronic acid derivatives,^{4,5} cyanide-induced aggregation of quantum dots,⁶ and hydrogen bonding interactions⁷ for the construction of cyanide anion sensors have been reported. On the other hand, a number of

fluorescent chemodosimeters have been developed based on specific chemical reactions.⁸ Although these chemodosimeters for cyanide have the advantage of high selectivity due to the minimized interference of other anions, they may still suffer from the high detection limit and decreased reaction rate in aqueous medium.^{8*k-m*} In addition, sensors displaying both ratiometric and colorimetric response to cyanide are able to offer quantitative information *via* their internal calibration of dual emissions/excitations and show the presence of CN^- *via* the altered color simultaneously. However, there are very few chemodosimeters exhibiting both ratiometric and colorimetric response to cyanide in aqueous solution.^{8*m-p*} Therefore, the design of a ratiometric and colorimetric chemodosimeter for cyanide the quantitative detection of cyanide in the aqueous solution remains challenging. Herein, we report a coumarin–hemicyanine hybrid fluorophore, **Cou-BT**, which exhibits the specific ratiometric and colorimetric response towards cyanide anion in aqueous acetonitrile solution.

Results and discussion

Design and synthesis of Cou-BT

Coumarin–hemicyanine hybrids are often exploited as fluorophore for chemosensors due to their relatively large Stokes shift and long emission wavelength.⁹ Moreover, the emission of the coumarin chromophore would be recovered due to the inhibition of π -conjugation between the half cyanine and coumarin induced by certain chemical reactions.^{9*b*} Therefore hybrid coumarin–hemicyanine derivatives are valuable platforms for the construction of ratiometric fluorescent sensors. The synthesis of **Cou-BT** is depicted in Scheme 1. The starting materials 7-diethylamino-2-aldehyde-coumarin and 3-carboxymethyl-2-methylbenzothiazole-3-ium

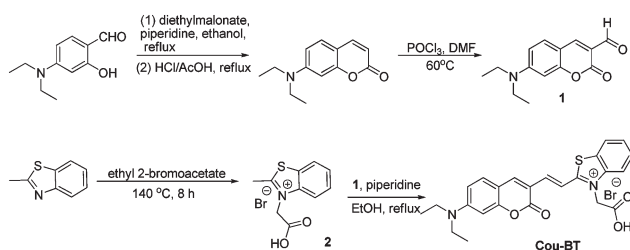
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Scheme 1 Synthesis of Cou-BT.

bromide were synthesized according to the reported procedures.¹⁰ **Cou-BT** was synthesized by conjugating compound 1 and compound 2 in the presence of piperidine as a catalyst. Compared with 7-dimethyl-2-aldehyde-coumarin, **Cou-BT** should display an emission shift to a longer wavelength due to the expanded π -conjugation and enhanced ICT progress from coumarin moiety to benzothiolium group. Considering the intrinsic nature of high electron deficiency on the 2-C atom of benzothiolium, it is expected that the cyanide anion might be able to attack this carbon atom, and this nucleophilic addition will not only interrupt the π -conjugation in the molecule of **Cou-BT**, but also block the ICT progress from coumarin moiety to benzothiolium group. As a result, both the absorption and emission of coumarin moiety should be recovered to those of coumarin derivative, displaying the expected ratiometric and colorimetric response to cyanide anion.

UV-vis absorption and emission spectra of Cou-BT

As shown in Fig. 1, free **Cou-BT** in aqueous acetonitrile solution ($\text{CH}_3\text{CN}-\text{H}_2\text{O} = 9:1, \text{v}:\text{v}$) exhibits one main absorption band centered at 543 nm ($\epsilon = 3.1 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$), which can be assigned to the ICT band of **Cou-BT**. When cyanide anion was added, distinct reduction of this band was observed, accompanied by the increase of a new band centered at 455 nm ($1.4 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$). This evident hypsochromic shift of the ICT band from 543 to 455 nm suggests that the π -conjugation and ICT progress of **Cou-BT** were both inhibited by the nucleophilic addition of cyanide to **Cou-BT**. Moreover, 5 equiv. cyanide is sufficient to make this nucleophilic addition be completed within 2 min, and the calculated pseudo-first-order rate constant (k') for cyanide anion addition was $(2.13 \pm 0.08) \times 10^{-2} \text{ s}^{-1}$.¹¹ This result suggests that **Cou-BT** is highly reactive to cyanide anions.

Cou-BT shows two characteristic fluorescence bands at 488 and 624 nm in the emission spectrum, respectively. The emission band at 624 nm is attributed to the ICT emission band, while the emission band at 488 nm should be ascribed to the diethylamino coumarin moiety. The intensity of the emission band at 624 nm is significantly decreased upon gradual addition of cyanide anion to **Cou-BT**, in the mean time, the increased intensity of the emission band at 488 nm was observed. The CN^- induced emission shift from 624 nm (pink) to 488 nm (bluish-green) also indicates that the π -conjugation and ICT effect of **Cou-BT** were both destroyed after cyanide anion addition. Additionally, the emission intensity ratio at 488 and 624 nm showed a drastic change from 2.6 to 29.8 in the presence of 5 equiv. of cyanide anion. The detection limit was estimated to be $0.64 \mu\text{M}$ at $S/N = 3$.

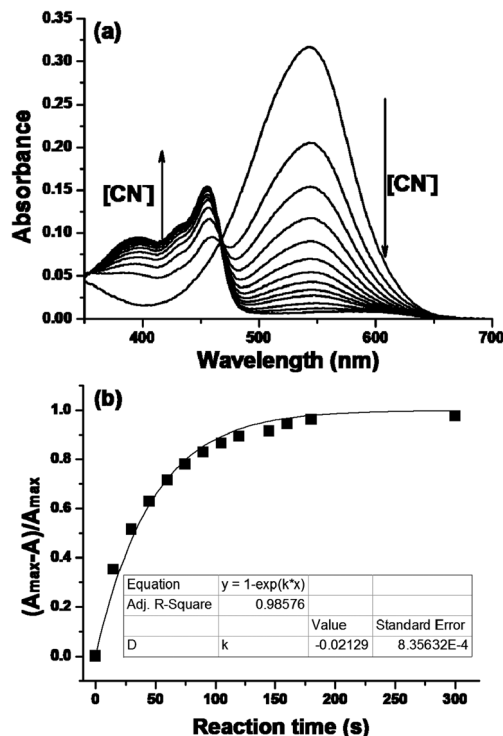


Fig. 1 (a) UV-vis spectra of **Cou-BT** ($1 \times 10^{-5} \text{ M}$) obtained at different time after the addition of 5 equiv. cyanide anion in $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (9:1, v:v) at 25 °C; (b) the temporal profile of absorption at $\lambda_{\text{abs}} = 543 \text{ nm}$ observed from the reaction between **Cou-BT** and cyanide anion (■). The red curve overlaid on the experimental data points is theoretical fit generated using $k' = (2.13 \pm 0.08) \times 10^{-2} \text{ s}^{-1}$.

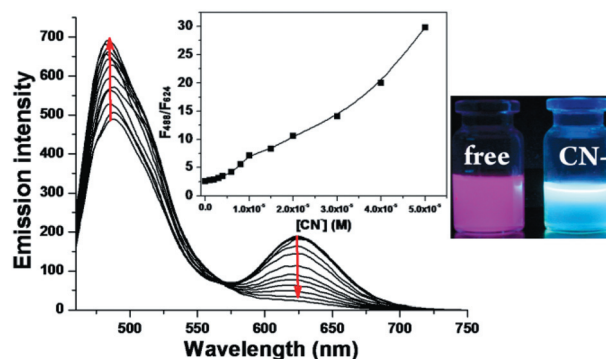


Fig. 2 Fluorescence responses of **Cou-BT** ($1 \times 10^{-5} \text{ M}$) toward different concentrations of cyanide anion in $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (9:1, v:v) at 25 °C. Each spectrum was obtained after cyanide anion addition for 2 min (Inset: titration profile based on the emission ratio at 488 and 624 nm, F_{488}/F_{624}).

Obviously, **Cou-BT** is a promising fluorescence ratiometric sensor for the detection of low level cyanide anion in samples (Fig. 2).

Selective detection of cyanide anion

The selective response of **Cou-BT** towards cyanide anion was evaluated by adding 5 equiv. of various anions such as F^- , Cl^- , Br^- , I^- , AcO^- , H_2PO_4^- , SCN^- , OCN^- , S^{2-} and HS^- ,

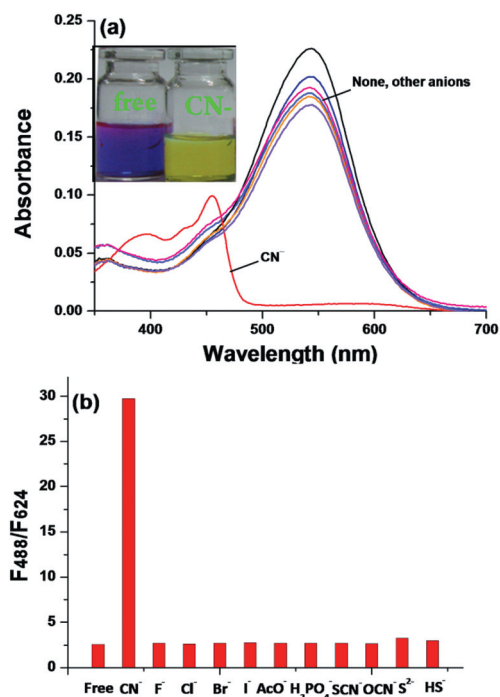


Fig. 3 (a) UV-vis spectra of **Cou-BT** (1×10^{-5} M) obtained upon the addition of 5 equiv. of various anions in $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (9 : 1, v : v). Each spectrum was obtained after mixing at 25 °C for 5 min. (b) Emission ratio at 488 and 624 nm, F_{488}/F_{624} , of **Cou-BT** (1×10^{-5} M) determined upon the addition of various analytes (5 equiv.) in $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (9 : 1, v : v).

respectively. As shown in Fig. 3, the absorption band at 544 nm of **Cou-BT** is slightly decreased in all these cases. Different from the distinct color change from violet to yellow-green, which is associated with the reaction between **Cou-BT** and cyanide anion, no significant color change was observed by addition of other anions (Fig. 3a inset). The selective fluorescence response of **Cou-BT** to cyanide anion was also investigated (Fig. 3b). As expected, almost no emission intensity ratio (F_{488}/F_{624}) changes were observed in the presence of F^- , Cl^- , Br^- , I^- , AcO^- , H_2PO_4^- , SCN^- , OCN^- , S^{2-} and HS^- .

Rationalization of the photophysical properties of **Cou-BT**

To investigate the mechanism of the ratiometric and colorimetric response of **Cou-BT** to cyanide anions, DFT calculations were carried out for **Cou-BT** and **Cou-BT-CN⁻** with 6-31G* basis sets using a suite of Gaussian 03 programs.¹² The optimized structures of **Cou-BT** and **Cou-BT-CN⁻** were shown in Fig. 4. The diethylamino coumarin and benzothiolium groups of **Cou-BT** are well planned *via* a conjugated bridge ($-\text{C}=\text{C}-$), the dihedral angle between the diethylamino coumarin and benzothiolium group is 2°. The addition of cyanide anion to 2-C atom of benzothiolium ring inhibited the plantation of diethylamino coumarin and benzothiolium groups, and the dihedral angle between diethylamino coumarin and benzothiolium groups of the reaction product **Cou-BT-CN⁻** is 100.3°. This structural difference between **Cou-BT** and **Cou-BT-CN⁻** shows the significant difference in π -conjugation between **Cou-BT** and **Cou-BT-CN⁻**.

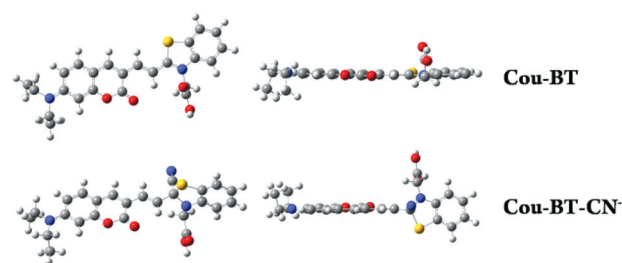


Fig. 4 Optimized structure of **Cou-BT** and **Cou-BT-CN⁻**.

Table 1 Calculated HOMOs and LUMOs of **Cou-BT** and **Cou-BT-CN⁻** and electronic contributions to the excitation of **Cou-BT** and **Cou-BT-CN⁻**

	Molecular orbitals	Electronic contribution of transition
Cou-BT		HOMO → LUMO 100%
Cou-BT-CN⁻		HOMO - 1 → LUMO 100%

Detailed information regarding the distinct absorption and emission blue shift upon the formation of **Cou-BT-CN⁻** can be obtained from TDDFT (time-dependent DFT) calculations as well. The calculated excitation wavelengths of **Cou-BT** and **Cou-BT-CN⁻** are 2.43 eV/509 nm and 3.26 eV/380 nm, respectively, which are slightly lower but in good agreement with the determined ones, and the simulated absorption spectra of **Cou-BT** and **Cou-BT-CN⁻** were shown in Fig. S3.† The calculated molecular orbitals and the electronic contribution of transition are shown in Table 1. In **Cou-BT** and **Cou-BT-CN⁻**, HOMO → LUMO and HOMO - 1 → LUMO transitions contribute respectively 100% to the excitation of **Cou-BT** and **Cou-BT-CN⁻**. From the LUMO of **Cou-BT**, it is clear that the ICT progress takes place through a conjugated bridge between the diethylamino coumarin and benzothiolium groups, while this is obviously prohibited in **Cou-BT-CN⁻** due to the cyanide anion addition. This result suggests that the absorption and emission blue shift from **Cou-BT-CN⁻** ascribed to its weakened ICT process relative to that in **Cou-BT**.

Conclusions

In summary, we have described a new ratiometric and colorimetric sensor for cyanide, **Cou-BT**, with a sensing mechanism of nucleophilic addition of cyanide anion to benzothiolium group of a coumarin-hemicyanine hybrid dye. **Cou-BT** shows a remarkable dual channel response in absorption and emission specifically for cyanide anion over other common anions in aqueous acetonitrile. **Cou-BT** is highly reactive to cyanide anion and the pseudo-first-order rate constant for cyanide addition was determined as $(2.13 \pm 0.08) \times 10^{-2} \text{ s}^{-1}$ at 298 K. The detection

limit was estimated to be 0.64 μM . DFT and TDDFT calculations suggest that the colorimetric and ratiometric sensing behavior of **Cou-BT** for cyanide anion was due to the interrupted π -conjugation and blocked ICT progress induced by cyanide addition to **Cou-BT**.

Experimental section

Materials and general methods

All reagents were obtained from commercial suppliers and used without further purification unless otherwise indicated. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury-plus 400M spectrometer and referenced to the residual proton signals of the solvent. Mass spectra were measured with a LCQ (ESI-MS, Thermo Finnigan) mass spectrometer. UV-vis absorption spectra were carried out on a Shimadzu UV-160U spectrophotometer. Fluorescence spectra were measured on a Perkin Elmer LS55 luminescence spectrophotometer (the pathlength of the quartz cell is 1 cm) with a xenon arc lamp as the light source.

All the stock solutions of anions (1.2 mM) were prepared with corresponding tetrabutylammonium or sodium salts in acetonitrile. A stock solution of **Cou-BT** (1.84 mM) was prepared in acetonitrile. The solution of **Cou-BT** was then diluted to 10 μM with acetonitrile and water (9 : 1, v : v). In titration experiments, 3 mL solution of **Cou-BT** (10 μM) was filled in a quartz optical cell of 1 cm optical path length, and the cyanide anion stock solution was added into the cuvette gradually by using a micropipette. To determine the sensing selectivity, the test samples were prepared by adding anions stock solution (5 equiv.) into 3 mL solution of **Cou-BT** (10 μM).

Synthesis of Cou-BT

A mixture of 7-dimethyl-2-aldehyde-coumarin (0.9 g, 3.7 mmol), piperidine (0.015 g, 0.185 mmol), 3-(carboxymethyl)-2-methylbenzothiazol-3-ium bromide (1.16 g, 3.7 mmol) in 20 mL ethanol was refluxed for 6 h. After being cooled to room temperature, the resulting precipitate was filtered, washed with ethanol and dried *in vacuo*, and **Cou-BT** was obtained as a dark-green solid (1.37 g, 85%). M.p. 236–238 $^{\circ}\text{C}$. ^1H NMR (400 M, CD_3OD), δ 8.33 (s, 1H), 8.19–8.17 (d, 1H, $J = 7.85$), 8.06–8.02 (m, 4H), 7.82–7.78 (t, 1H, $J = 7.36$), 7.73–7.69 (t, 1H, $J = 7.56$), 7.54–7.52 (d, 1H, $J = 9.04$), 6.87–6.84 (dd, $J_1 = 2.52$, $J_2 = 9.10$), 5.46 (s, 2H), 3.58–3.54 (q, 4H, $J = 7.18$), 1.27–1.23 (t, 6H, $J = 7.08$). ^{13}C NMR could not be obtained because of its poor solubility. ESI-MS: m/z , cal. 435.14, found, 435.25. Element analysis (%): cal. $\text{C}_{24}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$ C, 66.19, H, 5.32, N, 6.43. found, C, 66.46, H, 5.01, N, 6.56.

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Notes and references

- (a) G. C. Miller and C. A. Pritsos, *Cyanide: Soc., Ind. Econ. Aspects, Proc. Symp. Annu. Meet. TMS*, 2001, 73–81; (b) K. W. Kulig, *Cyanide Toxicity*, U. S. Department of Health and Human Services, Atlanta, GA, 1991.
- Guidelines for Drinking-Water Quality*, World Health Organization, Geneva, 1996.
- Z. Xu, X. Chen, H. N. Kim and J. Yoon, *Chem. Soc. Rev.*, 2010, **39**, 127.
- (a) Y. H. Kim and J. I. Hong, *Chem. Commun.*, 2002, 512; (b) X. Chen, S.-W. Nam, G.-H. Kim, N. Song, Y. Jeong, I. Shin, S. K. Kim, J. Kim, S. Park and J. Yoon, *Chem. Commun.*, 2010, **46**, 8953; (c) C.-F. Chow, M. H. W. Lam and W.-Y. Wong, *Inorg. Chem.*, 2004, **43**, 8387.
- (a) R. Badugu, J. R. Lakowicz and C. D. Geddes, *J. Am. Chem. Soc.*, 2005, **127**, 3635; (b) J. V. Ros-Lis, R. Martínez-Máñez and J. Soto, *Chem. Commun.*, 2005, 5260; (c) R. Badugu, J. R. Lakowicz and C. D. Geddes, *Dyes Pigm.*, 2005, **64**, 49; (d) Y. Kim, H.-S. Huh, M. H. Lee, I. L. Lenov, H. Zhao and F. P. Gabbai, *Chem.-Eur. J.*, 2011, **17**, 2057.
- W. J. Jin, M. T. Fernández-Argüelles, J. M. Costa-Fernández, R. Pereiro and A. Sanz-Medel, *Chem. Commun.*, 2005, 883.
- (a) S.-S. Sun and A. J. Lees, *Chem. Commun.*, 2000, 1687; (b) H. Miyaji and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2001, **40**, 154; (c) P. Anzenbacher, D. S. Tyson, K. Jursikova and F. N. Castellano, *J. Am. Chem. Soc.*, 2002, **124**, 6232.
- (a) J. V. Ros-Lis, R. Martínez-Máñez and J. Soto, *Chem. Commun.*, 2002, 2248; (b) M. Tomasulo, S. Sortino, A. J. P. White and F. M. Raymo, *J. Org. Chem.*, 2006, **71**, 744; (c) J. Q. Ren, W. H. Zhu and H. Tian, *Talanta*, 2008, **75**, 760; (d) F. Garcia, J. M. Garcia, B. Garcia-Acosta, R. Martínez-Máñez, F. Sancenon and J. Soto, *Chem. Commun.*, 2005, 2790; (e) Y. K. Yang and J. Tae, *Org. Lett.*, 2006, **8**, 5721; (f) D. Ryu, E. Park, D. S. Kim, S. Yan, J. Y. Lee, B. Y. Chang and K. H. Ahn, *J. Am. Chem. Soc.*, 2008, **130**, 2394; (g) Y. M. Chung, B. Raman, D.-S. Kim and K. H. Ahn, *Chem. Commun.*, 2006, 186; (h) D. G. Cho, J. H. Kim and J. L. Sessler, *J. Am. Chem. Soc.*, 2008, **130**, 12163; (i) J. L. Sessler and D. G. Cho, *Org. Lett.*, 2008, **10**, 73; (j) Y. Chung, H. Lee and K. H. Ahn, *J. Org. Chem.*, 2006, **71**, 9470; (k) S.-J. Hong, J. Yoo, S.-H. Kim, J. S. Kim, J. Yoon and C.-H. Lee, *Chem. Commun.*, 2009, 189; (l) G.-J. Kim and H.-J. Kim, *Tetrahedron Lett.*, 2010, **51**, 185; (m) X. Wu, B. Xu, H. Tong and L. Wang, *Macromolecules*, 2011, **44**, 4241; (n) L. Yuan, W. Lin, Y. Yang, J. Song and J. Wang, *Org. Lett.*, 2011, **13**, 3730; (o) X. Lv, J. Liu, Y. Liu, Y. Zhao, M. Chen, P. Wang and W. Guo, *Org. Biomol. Chem.*, 2011, **9**, 4954; (p) Z. Liu, X. Wang, Z. Yang and W. He, *J. Org. Chem.*, 2011, **76**, 10286.
- (a) J.-A. Richard, M. Massonneau, P.-Y. Renard and A. Romieu, *Org. Lett.*, 2008, **10**, 4175–4178; (b) L. Yuan, W. Lin and J. Song, *Chem. Commun.*, 2010, **46**, 7930–7932.
- (a) J.-S. Wu, W.-M. Liu, X.-Q. Zhuang, F. Wang, P.-F. Wang, S.-L. Tao, X.-H. Zhang, S.-K. Wu and S.-T. Lee, *Org. Lett.*, 2007, **9**, 33; (b) S. Tatay, P. Gaviña, E. Coronado and E. Palomares, *Org. Lett.*, 2006, **8**, 3857.
- T. J. Dale and J. Rebek, *J. Am. Chem. Soc.*, 2006, **128**, 4500.
- M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *Gaussian 03*, Gaussian Inc., Wallingford CT, 2004.