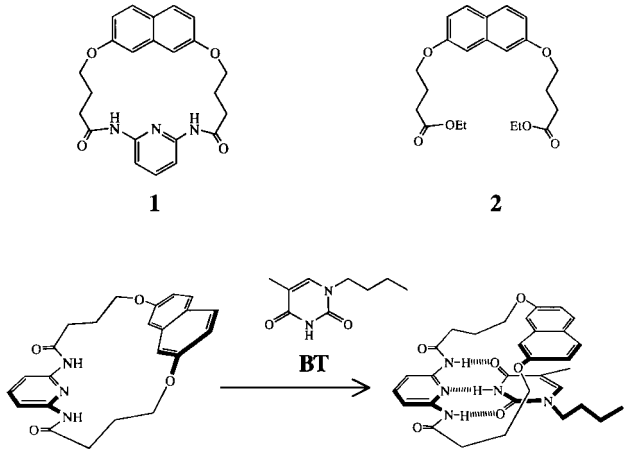
Spectroscopic Evidence for Cooperative Binding of a Host in Molecular Hinge

Noboru Kitamura,* Yusuke Suzuki, Masahiro Chiba, Norio Sakata, and Haeng-Boo Kim#
Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060-0810

(Received April 27, 2001;CL-010388)

Recognition of a thymine derivative by a molecular-hinge type compound was investigated on the basis of absorption and fluorescence spectroscopies. Spectroscopic evidence for hydrogen-bonding and charge-transfer interactions in molecular recognition was demonstrated.

A "molecular hinge (**1**)", reported by Hamilton and Engen in 1987, possesses a unique macrocyclic structure, in which naphthyl and 2,6-diaminopyridine moieties are linked via C3-alkyl chains as shown in Scheme 1.[1] An interesting property of the compound is a large conformational change upon recognition of thymine (1-butylthymine: **BT**)[1] or flavin derivatives[2,3] with the diaminopyridine group in **1** through triple hydrogen-bonding. Besides the hydrogen-bonding interaction, although the van der Waals interaction between the naphthyl group of **1** and **BT** has been suggested, a further study on the system has not been reported. The molecular structures suggest that electronic interactions between **1** and **BT** should reflect on absorption and/or fluorescence characteristics of **1**. Since fluorescence sensing in molecular or ion recognition is of primary importance for advances in sensitive diagnosis of various compounds,[4] detailed spectroscopic investigations of the **1**:**BT** system are worth exploring. In this letter, we report direct evidence of cooperative binding of **BT** by **1**.



Scheme 1.

Compounds **1** and **BT** were prepared according to the literatures[1,5] and their structures were confirmed by ^{1}H NMR and elemental analysis. A naphthalene derivative (**2**) was also studied as a model for **1** without a hydrogen-bonding ability. Spectroscopic measurements were conducted in $CHCl_3$. Figure 1 shows absorption spectra of **1** in the absence and presence of **BT**. The absorption band at around 328 nm in the absence of **BT** was assigned to the electronic transition of the naphthyl group in **1**. As seen in Figure 1, an addition of **BT** ($(1.0–20) \times 10^{-3}$ M (= mol/dm^3)) to a $CHCl_3$ solution of **1** resulted in a decrease in the absorbance at 328 nm and, this accompanied an appearance of a new band at 331 nm as well as an increase in the absorption intensity in the wavelength (λ) region shorter than 325 nm. Under analogous experimental conditions, the absorption spectrum of **2** did not show any change even in the presence of **BT** up to 2.0×10^{-2} M. Therefore, the spectral changes in Figure 1 are essentially due to recognition of **BT** by the diaminopyridine group in **1** through hydrogen-bonding and simultaneous molecular interactions between **BT** and the naphthyl group in **1**. Observations of clear isosbestic points at 326 and 330 nm also indicate stoichiometric binding of **1** with **BT**. On the basis of the results in Figure 1 and analytical equations,[6] we determined the stability constant (K) of the **1**:**BT** complex as $K = 1 \times 10^3$ M^{-1}. Although the K value is ~3 times larger than that determined by NMR (290 M^{-1}),[1] we think that the value determined by the absorption spectra would be more reliable than that by NMR.

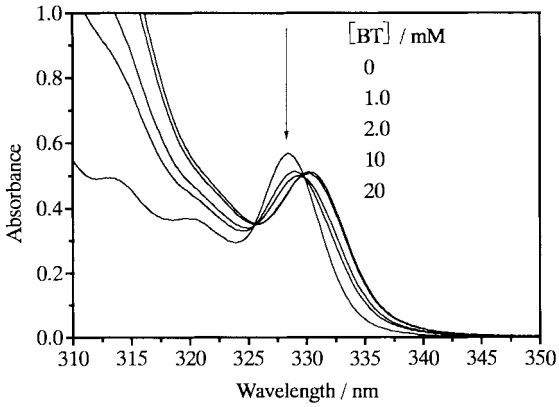


Figure 1. Absorption spectra of **1** (0.21 mM) in the absence and presence of **BT** in chloroform.

Fluorescence spectral responses of **1** upon recognition of **BT** in $CHCl_3$ are shown in Figure 2. Structured fluorescence observed for **1** in $320 < \lambda < 360$ nm is responsible for the monomer excited-state of the naphthyl group. An addition of **BT** brought about fluorescence quenching of **1**, while the excited-state of **2** was not quenched by **BT**, which agreed very well with the results by absorption spectroscopy. In the case of **1**, furthermore, fluorescence quenching accompanied an appearance of broad and structureless band at around $\lambda \sim 420$ nm, with an isoemissive point being observed at 380 nm. Information about fluorescence quenching and the molecular interaction was also provided by the fluorescence dynamics of **1** (Figure 3, excitation and monitoring wavelengths were 315 and 340 nm, respectively). Although the fluorescence of **2** showed a single exponential decay with a time constant (τ_1) of 1.3 ns

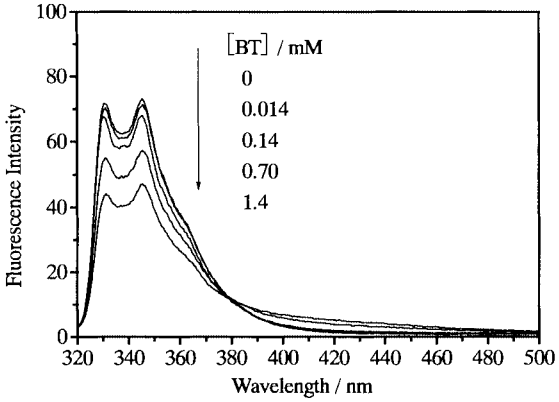


Figure 2. Fluorescence spectra of **1** (0.21 mM) in the absence and presence of **BT** in chloroform.

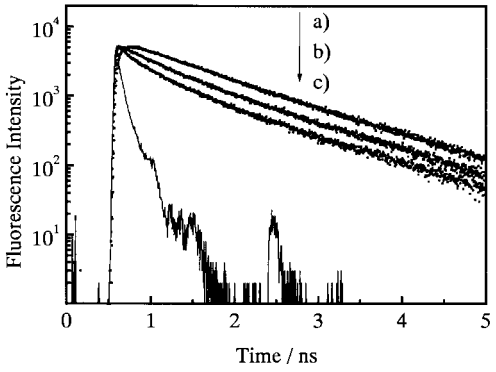


Figure 3. Fluorescence decay profiles of **1** (25 μM) in the absence of **BT**[**a**)] and the presence of **BT**[**b**) **1**:**BT**=1:100], and [**c**) **1**:**BT**=1:200] in chloroform.

(data are not shown), that of **1** in the absence of **BT** exhibited a double exponential decay with τ_1 = 1.2 and τ_2 = 0.6 ns. The τ_1 component could be assigned to the non-interacted naphthyl group in **1** due to the similarity to the decay time of **2** (1.3 ns), while the τ_2 component would be indicative of the electronic interaction between the naphthyl and diaminopyridine groups in **1**. In the presence of **BT**, on the other hand, the fluorescence decay of **1** became faster as compared with that without **BT**: quenching of the excited-state of **1** by **BT**. However, the decay was fitted by a triple exponential function with τ_1 = 1.2, τ_2 = 0.4, and τ_3 = 0.06 ns. Within an experimental error, the τ_1 and τ_2 values were essentially the same with those observed for **1** without **BT**. The very short τ_3 component will be originated from the electronic interaction between **1** and **BT**. In practice, when the fluorescence was monitored at 400 nm, the contribution of the τ_3 component to the overall decay was larger than that determined at 340 nm, indicating τ_3 is responsible for the band at around $\lambda \sim 420$ nm. Fluorescence quenching and the new fluorescence band of **1** in the presence of **BT** are thus concluded to be originated from hydrogen-bonding and molecular interactions in the host–guest complex.

An electronic interaction in the complex has been suggested by X-ray crystallography; the naphthyl ring lies approximately parallel to the plane of **BT** at a closest inter-plane distance of 3.37 Å.[1] Nonetheless, there is no information about nature of the electronic interaction. The broad fluorescence band at around $\lambda \sim 420$ nm suggests a charge-transfer (CT) interaction between **1** and **BT**. Therefore, we conducted electrochemical measurements of the derivatives in CH_3CN. The oxidation potential ($E_{1/2}(D^+/D)$) of the naphthyl group in **1** or **2** was determined to be 1.41 or 1.33 V (vs Ag/AgCl), respectively, while **BT** was reduced at $E_{1/2}(A/A^-) = -1.71$ V. A free energy change of the CT interaction in CH_3CN (ΔG) was then calculated to be –55 or –62 kJ/mol for the **1–BT** or **2–BT** system, respectively. These values were negative enough for the CT interaction between the naphthyl group and **BT**.[7] At the present stage of the investigation, although we have not conducted electrochemical measurements of the **1**:**BT** complex, the redox potentials of the naphthyl group and **BT** would vary to some extent upon complexation. Nonetheless, exothermic nature of the CT interaction in the **1**:**BT** pair could be held even by the participation of the hydrogen-bonding interaction. In the case of the **1**:**BT** complex in $CHCl_3$, therefore, the CT interaction renders fluorescence quenching of **1** and the appearance of the new fluorescence at around $\lambda \sim 420$ nm. For the **2–BT** system, on the other hand, although the ΔG value indicates that the fluorescence of **2** should be quenched by **BT**, no fluorescence quenching was observed. This is readily understood by the very short excited-state lifetime of **2**. Since ΔG is largely negative, fluorescence quenching would proceed in a diffusion-controlled rate, $\sim 10^{10}$ M^{-1} s^{-1}. According to the Stern–Volmer equation, the concentration of **BT** should be > 0.1 M for efficient fluorescence quenching of **2** to be observed. Despite the short excited-state lifetime of **1**, on the other hand, efficient fluorescence quenching by **BT** proceeds. Thus, it comes to the conclusion that hydrogen-bonding of **1** with **BT** and simultaneous CT interaction between the naphthyl group and the π system of **BT** in the ground-state take place cooperatively, and excitation of the host–guest complex renders efficient quenching of the excited-state of **1**. Cooperative binding of **BT** with **1** was proved directly for the first time by steady-state and dynamic molecular spectroscopy.

N. K. thanks a Grant-in-Aid from the Ministry of Education, Science, Sports and Culture, Japan (No. 11440215) for partial support of the research.

References and Notes

Present address: Engineering Research Institute, Faculty of Engineering, The University of Tokyo, 2-11-16, Yayoi, Bunkyo-ku, Tokyo 113-8656.
1 A. D. Hamilton and D. V. Engen, *J. Am. Chem. Soc.*, **109**, 5035 (1987).
2 S. Shinkai, G.-X. He, T. Matsuda, A. D. Hamilton, and H. S. Rosenzwig, *Tetrahedron. Lett.*, **30**, 5895 (1989).
3 N. Tamura, K. Mitsui, T. Nabeshima, and Y. Yano, *J. Chem. Soc., Perkin Trans, 2*, **1994**, 2229.
4 J. P. Desvergne and A. W. Czarnik, "Chemosensors of Ion and Molecular Recognition," Kluwer Academic Press, Dordrecht (1997).
5 D. T. Brown, in "Synthetic Procedures in Nucleic Acid Chemistry," ed. by W. W. Zorbach and R. S. Tipson, Wiley-Interscience, New York, 1968; p. 98.
6 a) C. S. Wilcox and M. D. Cowart, *Tetrahedron Lett.*, **27**, 5563 (1986). b) N. Balabai, B. Linton, A. Napper, S. Priyadarshy, and D. H. Waldeck, *J. Phys. Chem. B*, **102**, 9617 (1998).
7 R. D. Cannon, "Electron Transfer Reactions," Butterworths, London,1980.