

An Azacrowned Phthalimide as a Metal-Ion Sensitive and Solvatofluorochromic Fluorophore: Fluorescence Properties and a Mimic Integrated Logic Operation

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The novel azacrowned phthalimide **1** has been prepared and its fluorescence properties have been investigated by addition of EtOH and Ag^+. The phthalimide **1** showed appreciable solvatofluorochromism; its fluorescence maxima (λ_{FL}) appeared in the wavelength region between 458 (in Et_2O) and 544 nm (in EtOH). In benzene, the phthalimide **1** gave off blue emission (λ_{FL} 466 nm) while it emitted green fluorescence (λ_{FL} 497 nm) upon addition of 250 mM of EtOH. Both the blue and the green emissions were quenched by Ag^+. Potential logic operations of the phthalimide **1** were examined using fluorescence outputs at 450 (Out_1) and 515 nm (Out_2) and two input stimuli, EtOH (In_1) and Ag^+ (In_2). The Out_1 was *on* in the absence of these inputs while its intensity was reduced (*off*) by either or both of the inputs to serve as a NOR operator. The Out_2 was *off* without the inputs; in contrast, the intensity of Out_2 was enhanced (*on*) by In_1. The enhanced Out_2 was switched *off* by In_2. The Out_2, thus, corresponds to an INHIBIT operation responding to the input signals. The crowned phthalimide **1** mimics a two-input–two-output combinational logic gate with a single fluorophore and a single ion-sensing unit.

In the past two decades, a great number of chemosensors have been developed by means of combinations of host functions with chromophores,[1,2] fluorophores,[3,4] or chemiluminophores.[5] Such chemosensors have been applied to molecular photodevices as well as analytical tools.[6,7] They have become increasingly attractive materials from the aspect of logic gates on the molecular level[6–9] since the pioneering work by de Silva.[10] Molecular logic gates displaying basic logic operations (NOT, OR, AND, NOR, NAND, XOR, and XNOR) and simple combinational ones (INHIBIT and ENOR) have been reported.[11–19] Most of the conventional molecular logic gates possess a single chromophore and display switching of one output signal responding to specific input(s). More complex combinational logic circuits which reveal various outputs have also been reported. Molecular logic gates mimicking the half adder function have been constructed by using multi-chromophoric systems.[20,21] Multi-state photochromic materials have been also used as integrated molecular logic operators.[22–24] More recently, the hole-transport ability of DNA has been applied to a novel logic operation.[25]

Most conventional molecular logic operators with fluorescence output show a single luminescent output signal from the fluorophore incorporated. A multicolor probe, which displays a more complex logic operation, requires two or more signal-emitting components in order to show plural outputs. Solvatochromic and solvatofluorochromic dyes have received extensive interest because they can serve as probes for the microscopic environment of a medium.[26] It would also be of interest to apply such chromophores to a signaling unit in a molecular logic gate because they may display multiple output signals or alternation of output signals with a single chromophore depending on environmental conditions. Furthermore, when a host function is incorporated into such solvent-sensitive chromophores, it is expected that one can control the output of the chromophore not only by solvent effects but also by a specific guest. A few studies on chromophores displaying both solvent and guest sensitivities have been reported; however, very little information has been available about the cooperative effects of the inputs on modification of their absorption and/or fluorescence properties.[27,28]

According to the above concept, we have designed a novel aminophthalimide derivative **1** (Fig. 1a) in which the amino group is modified as an aza-15-crown-5 host function. It has been reported that 4-aminophthalimides display significant solvatofluorochromism due to their intramolecular charge-transfer (ICT) fluorescence.[29] Thus, one would expect that the azacrowned phthalimide **1** would display (i) modulation of the color of the fluorescence output (Fig. 1b, $h\nu_{FL}$) by means of solvent effects (Fig. 1b, In_1) and (ii) *on*/*off* switching of the fluorescence output(s) through modification of the ICT character upon binding with a metal cation (Fig. 1b, In_2). Herein, we report fundamental fluorescence properties of phthalimide **1** and modulation of its emission by solvent effects and metal cations. Additionally, a potential integrated logic operation of the crowned phthalimide **1** is described.

Results and Discussion

Preparation of Crowned Phthalimide 1. The crowned phthalimide **1** was prepared by the route shown in Scheme 1. When 4-amino-*N*-methylphthalimide **3** was reacted with pentaethylene glycol ditosylate under the usual *N*-alkylation conditions,[30] only the starting aminophthalimide **3** was recovered.

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Thus, aminophthalimide **3** was treated with sodium hydride at 60 °C in 1,4-dioxane, then, reacted with pentaethylene glycol ditosylate at 120 °C to afford the desired crowned phthalimide **1** in a reasonable yield (20%). The structure of the phthalimide **1** was confirmed by ^{1}H and ^{13}C NMR and mass spectra as well as by elemental analysis. Conventionally, an *N*-aryl-aza-15-crown-5 host function has been constructed by crowning of *N*,*N*-bis(2-hydroxyethyl)aniline with bis(2-chloroethyl) ether.[31] In the present case, the azacrown ring in phthalimide **1** could be conveniently prepared through the one-step crowning of the starting phthalimide **3**.

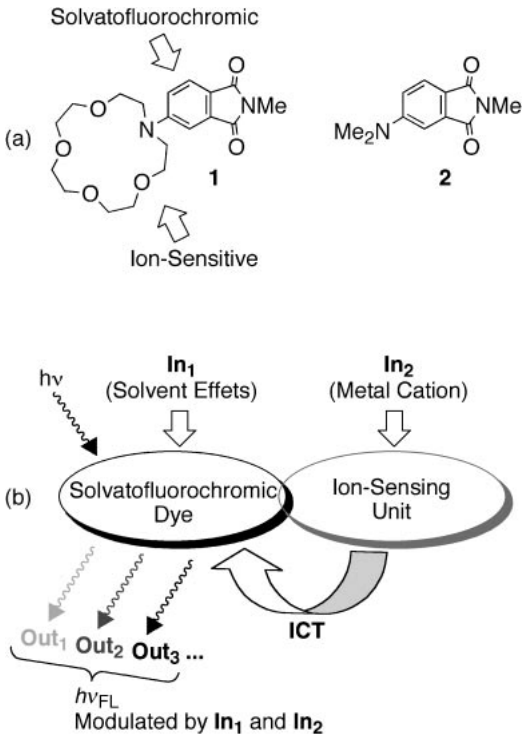
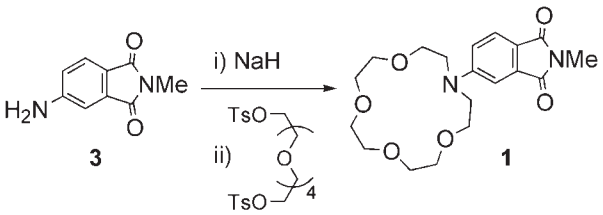


Fig. 1. (a) Molecular design of an azacrowned phthalimide **1** and (b) a concept for a multicolor fluorescence probe driven by both solvent effects (In_1) and metal cations (In_2) as input signals.

Solvent Effects on Absorption and Fluorescence Spectra of Crowned Phthalimide 1. In order to understand the fundamental spectroscopic properties of the crowned phthalimide **1**, its absorption and fluorescence spectra were measured in several solvents. Phthalimide **1** shows a broad absorption band around 390 nm. The absorption maxima (λ_{abs}) displayed moderate red shifts depending on solvent polarity in the region between 382 (in Et_2O) and 398 nm (in EtOH) as shown in Fig. 2a. The spectroscopic data are summarized in Table 1. On the other hand, the fluorescence of phthalimide **1** showed more appreciable solvent dependence as shown in Fig. 2b. The emission maxima (λ_{FL}) shifted from 458 (in Et_2O) to 544 nm (in EtOH) depending on the polarity of the solvent examined (Table 1). When the absorption and emission maxima were plotted against the microscopic solvent polarity function $E_T(30)$[32] (Fig. 3a), it was found that both maxima shifted to a lower energy region with increase of solvent polarity, and the bathochromic shift was more significant for the fluorescence than



Scheme 1. Preparation of azacrowned phthalimide **1**.

Table 1. Absorption (λ_{Abs}) and Fluorescence (λ_{FL}) Maxima and Fluorescence Quantum Yield of Crowned Phthalimide **1** in Various Solvents

Solvent	$E_T(30)$[a)]	λ_{Abs}/nm	λ_{FL}/nm	Φ_F
Benzene	34.3	387	466	0.73
Et_2O	34.5	382	458	0.63
AcOEt	38.1	386	472	0.65
$CHCl_3$	39.1	395	498	0.75
MeCN	45.6	391	500	0.27
EtOH	51.9	398	544	<0.04

a) Ref. 32.

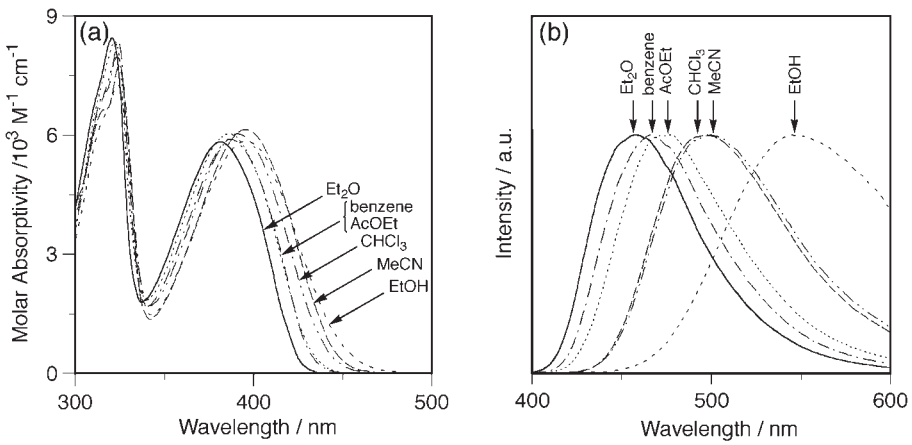


Fig. 2. (a) Electronic absorption and (b) fluorescence (normalized, λ_{ex} 380 nm) spectra of crowned phthalimide **1** in various solvents.

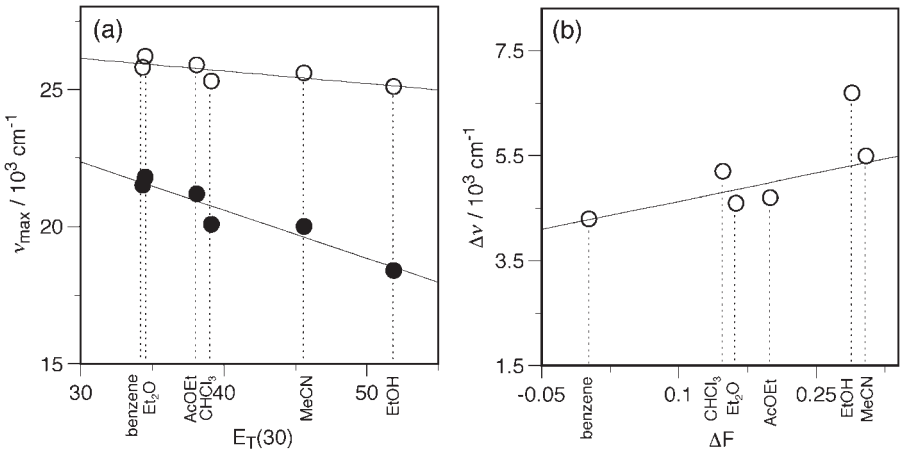


Fig. 3. (a) Correlations of absorption (○) and emission maxima (●) of phthalimide **1** with $E_T(30)$. (b) Lippert–Mataga's plot for phthalimide **1** (The point obtained in EtOH was not considered for the line fitting).

for the absorption. These results indicate that the emitting state of phthalimide **1** possesses ICT character, as in the case of 4-aminophthalimide derivatives without a crown ring.[28,33] The ICT characters were analyzed by Lippert–Mataga's equation (Eq. 1);[34]

$$\Delta\nu = \frac{2\Delta\mu^2}{hca^3}\Delta F + \text{const}, \quad (1)$$

$$\Delta F = \frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}, \quad (2)$$

where $\Delta\nu$ is the Stokes shift, $\Delta\mu$ refers to the difference of dipole moments between an excited and the ground states, a is the Onsager cavity radius, and ε and n are, respectively, dielectric constant and optical refractive index of the solvent. The experimental $\Delta\nu$ values were plotted as a function of ΔF (Eq. 2) as shown in Fig. 3b. From the slope of the plot, the change of dipole moment $\Delta\mu$ of phthalimide **1** was evaluated to be 3.8 D using a cavity radius $a = 3.37$ Å, which was estimated for 4-(dimethylamino)phthalimide.[33a] The $\Delta\mu$ value was comparable to that evaluated for 4-aminophthalimide derivatives (3.6–5.4 D).[33] These results indicate that the absorption and the fluorescence properties of phthalimide **1** are quite similar to those reported for 4-aminophthalimides.[33] Additionally, the fluorescence quantum yield of phthalimide **1** tended to decrease with increase of solvent polarity (Table 1) as in the case of 4-aminophthalimides which have no crown ring.[33] Therefore, we conclude that the crowning on the amino group provided minimal effects on the electronic nature of the 4-aminophthalimide luminophore in **1**, allowing it to display the desired solvent-dependent fluorescence color change.

Fluorescence Modulation of Crowned Phthalimide 1 by EtOH. The solvent effects on the fluorescence of phthalimide **1** indicate that the most significant bathochromic shift was caused by EtOH (cf. Table 1). It has been pointed out that hydrogen-bond-donating solvents caused effective bathochromic shifts of the fluorescence of 4-aminophthalimides not only by polar effects but also by hydrogen bonding at the carbonyl moieties of the chromophore.[33] Thus, it is expected that EtOH will serve as an input signal by which the fluorescence color of phthalimide **1** can be modified efficiently. Fluorescence modulation of phthalimide **1** by EtOH, as the input stimulus

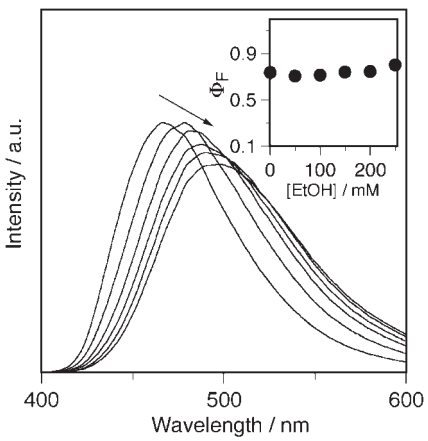


Fig. 4. Effect of EtOH (0–250 mM) on the fluorescence spectra of phthalimide **1** (1×10^{-5} M, λ_{ex} 380 nm). The inset shows fluorescence quantum yield of phthalimide **1** plotted as a function of [EtOH].

(Fig. 1, In_1), was investigated in order to reveal the potential of EtOH for alternation of the fluorescence wavelength.

When the fluorescence spectra of phthalimide **1** were measured in Et_2O or MeCN by titration with EtOH, no significant change in the fluorescence color was detected; only a slight red shift of λ_{FL} in Et_2O ($\Delta\lambda_{FL} \sim 8$ nm at [EtOH] = 120 mM) and moderate fluorescence quenching in MeCN ($I_F/I_{F_0} \sim 0.85$ at [EtOH] = 250 mM) were observed. In contrast, in benzene, addition of EtOH resulted in an appreciable bathochromic shift of the fluorescence, as shown in Fig. 4. The color of the fluorescence changed from blue (λ_{FL} 466 nm in the absence of EtOH) to green (λ_{FL} 497 nm at [EtOH] = 250 mM). As shown in the inset of Fig. 4, the fluorescence quantum yield of phthalimide **1** was almost constant irrespective of the [EtOH] investigated (≤250 mM). Therefore, EtOH was found to serve as an efficient input signal (Fig. 1, In_1) to control the fluorescence wavelength of phthalimide **1** without significant fluorescence quenching in benzene. In the case of the control compound **2**, red shift of fluorescence was also observed upon addition of EtOH. The λ_{FL} of phthalimide **2** was shifted from 466 to 498 nm by addition of 250 mM of EtOH in benzene. Such

effects of EtOH have been also reported for the fluorescence of 4-aminophthalimide.[33b]

Modulation of Fluorescence of Phthalimide 1 by Metal Cations. Fluorescence spectra of crowned phthalimide **1** were measured in the presence of several metal cations in order to find the second input (Fig. 1, In_2) by which the fluorescence intensity can be altered. Figure 5 shows the fluorescence spectra of phthalimide **1** in MeCN observed in the presence of metal cations. It was found that Ag^+ showed the most effective fluorescence quenching among the metal cations investigated (relative intensity at 500 nm; none:Li^+:Na^+:Mg^{2+}:Ag^+ = 100:87:57:23:8). Thus, we selected Ag^+ as the input signal for the fluorescence switching (Fig. 1b, In_2), and the effects of Ag^+ on the photophysical properties of phthalimide **1** were investigated. As Ag^+ (as perchlorate) is advantageously soluble in benzene, fluorescence modulation of phthalimide **1** by Ag^+ and by cooperative action of Ag^+ and EtOH can be examined in this solvent. On the other hand, harder alkali or alkali earth metal cations afforded complexes with phthalimide **1** which were insoluble in benzene; thus, they were not suitable as the input signal for the fluorescence modulation.

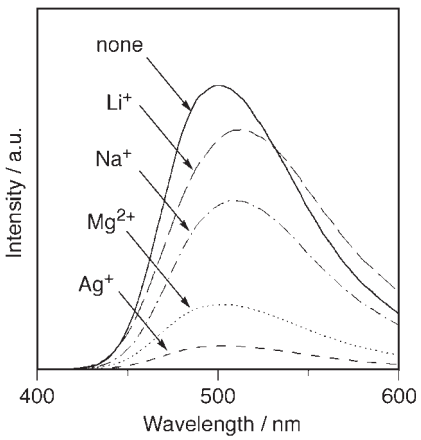


Fig. 5. Fluorescence emission spectra (λ_{ex} 400 nm) of the crowned phthalimide **1** (4×10^{-5} M, MeCN) in the presence of excess metal cations (>200 equiv as perchlorate).

Effects of Ag^+ on the Absorption Spectra of Phthalimide 1 in Benzene. The absorption spectra of phthalimide **1** observed by titration with Ag^+ (0–90 equiv) are shown in Fig. 6a. The intensity of the absorption band at 387 nm decreased with increase of [Ag^+], showing isosbestic points at 334 and 352 nm. These spectral changes indicate that phthalimide **1** and Ag^+ interact significantly in the ground state. The absorption spectra of 4-(dimethylamino)phthalimide **2**, as the control compound, are shown in Fig. 6b. The phthalimide **2** did not display any significant changes in the absorption spectra upon addition of Ag^+ ($\leq$90 equiv). Therefore, the azacrown host function of the modified phthalimide **1** plays an important role in association with Ag^+ in the ground state, and coordination of the nitrogen atom of the azacrown ring with Ag^+ suppressed the ICT transition of phthalimide **1**. The complex formation of crowned phthalimide **1** with Ag^+ in the ground state was analyzed by assuming 1:1 equilibrium between the ligand and Ag^+ (association constant K_a is described by Eq. 3). Change in absorption for the complex formation can be formulated as a function of $1/[Ag^+]$ by using the Benesi–Hildebrand method (Eq. 4):[35]

$$K_a = \frac{[\mathbf{1}\cdot Ag^+]}{[\mathbf{1}][Ag^+]}, \tag{3}$$

$$\frac{1}{\Delta Abs} = \frac{1}{\Delta\varepsilon K_a[\mathbf{1}]_0[Ag^+]} + \frac{1}{\Delta\varepsilon[\mathbf{1}]_0}, \tag{4}$$

where ΔAbs is change in absorbance of phthalimide **1** upon complex formation with Ag^+, $\Delta\varepsilon$ denotes the difference of molar extinction coefficient between free ligand **1** and complex **1**·Ag^+, and $[\mathbf{1}]_0$ is initial concentration of phthalimide **1**. By the least-square fitting of Eq. 4 to the observed absorbance change at 390 nm (ΔAbs_{390nm}), a linear correlation was obtained (Fig. 6a, inset). Therefore, the 1:1 complex formation between phthalimide **1** and Ag^+ is probable under the measurement conditions.[36] From the slope and the intercept of the plot, the association constant K_a was determined to be $1.4 \pm 0.14 \times 10^3$ M^{-1}.[37] The K_a value indicates that crowned phthalimide **1** associates moderately with Ag^+ in the ground state.

Modification of Fluorescence of Phthalimide 1 by Ag^+. As shown in Fig. 4, the color of the fluorescence of phthal-

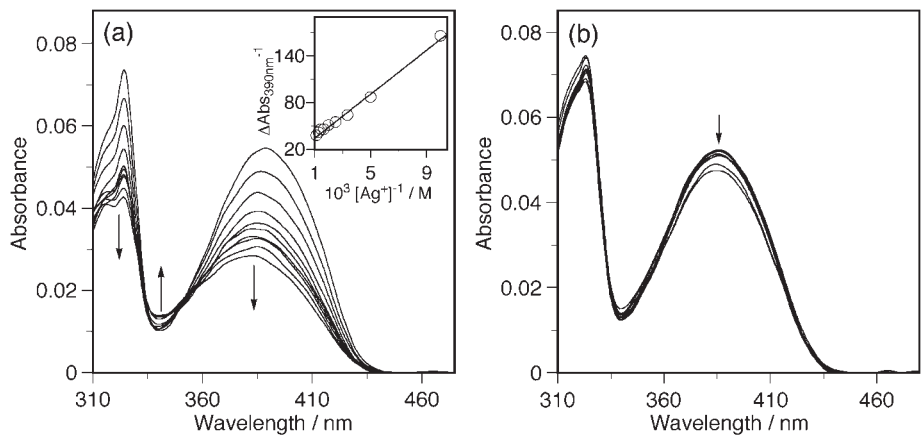


Fig. 6. Electronic absorption spectra of phthalimides **1** and **2** observed upon addition of Ag^+ (0–9×10^{-4} M) in benzene. (a) Crowned phthalimide **1** (1×10^{-5} M). Inset: plot of $1/\Delta Abs_{390nm}$ as a function of $1/[Ag^+]$ (Benesi–Hildebrand plot). (b) 4-(Dimethylamino)phthalimide **2** (1×10^{-5} M).

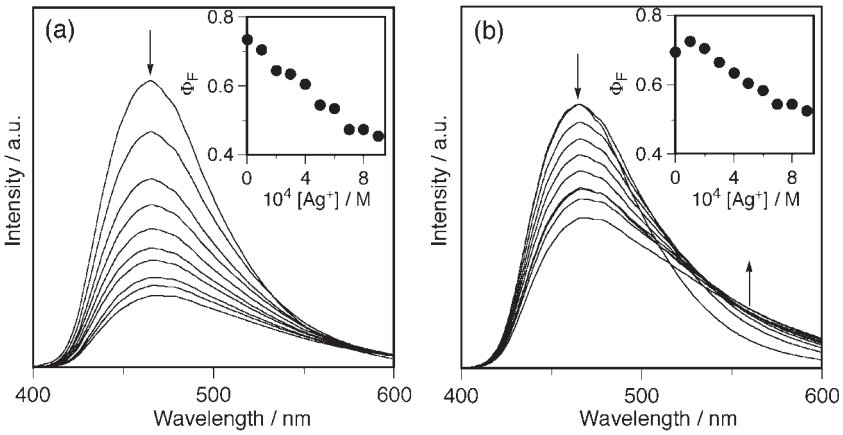


Fig. 7. Fluorescence spectra of phthalimides (a) **1** (1×10^{-5} M, λ_{ex} 380 nm) and (b) **2** (1×10^{-5} M, λ_{ex} 380 nm) observed upon addition of Ag^+ (0–9×10^{-4} M) in benzene. The insets show fluorescence quantum yield of the phthalimides plotted as a function of [Ag^+].

imide **1** can be modified by EtOH (blue in pure benzene and green in the presence of 250 mM of EtOH). In order to reveal whether Ag^+ displays efficient modulation of both blue and green emission, the fluorescence spectra of phthalimide **1** were measured in the presence of Ag^+ and for the coexistence of Ag^+ with EtOH.

Figure 7a shows the fluorescence spectra of crowned phthalimide **1** in benzene observed upon titration with Ag^+. The blue fluorescence emission was effectively quenched by Ag^+. In the presence of 90 equivalents of Ag^+, the intensity of the fluorescence was reduced to 25% of that observed in the absence of the additive. Thus, it was found that Ag^+ could switch off the fluorescence of phthalimide **1** in benzene. Figure 7b shows the fluorescence spectra of dimethylamino derivative **2** observed upon addition of Ag^+. The fluorescence of the control phthalimide **2** was moderately quenched by Ag^+; by addition of Ag^+ (90 equiv), the fluorescence intensity was reduced to 60% of that observed in the absence of the additive. As phthalimide **2** did not show any appreciable changes in the absorption spectra upon addition of Ag^+, the interaction of phthalimide **2** with Ag^+ in the ground state was not significant (Fig. 6b). Thus, the fluorescence quenching of phthalimide **2** by Ag^+ was considered to occur mainly through deactivation of the photoexcited phthalimde **2*** by Ag^+.[39] In contrast, in the case of the crowned phthalimide **1**, addition of Ag^+ caused a considerable decrease of the fluorescence quantum yield (Fig. 7a, inset) as well as a reduction of the intensity of the ICT absorption band (Fig. 6a). Therefore, crowned phthalimide **1** interacted with Ag^+ in both the ground and the excited states. Consequently, the fluorescence of phthalimide **1** was quenched by Ag^+ more efficiently than in the case of the control phthalimide **2**, through both the complex formation in the ground state (static quenching) and the deactivation of the photoexcited **1*** (dynamic quenching).[40]

In the fluorescence spectra of the control phthalimide **2**, an extra emission band appeared at around 560 nm upon addition of Ag^+ (Fig. 7b). If one considers the possibility of polycyclic aromatic compounds forming an exciplex with Ag^+,[41] the additional emission band might be ascribed to an exciplex between photoexcited phthalimide **2*** and Ag^+. In the case of crowned phthalimide **1**, such an effect was not pronounced (Fig. 7a). Therefore, we conclude that the interactions of the phthalimide **1** with Ag^+ occur in a different manner than those of the control phthalimide **2** in both the ground and the excited states (Figs. 6 and 7).

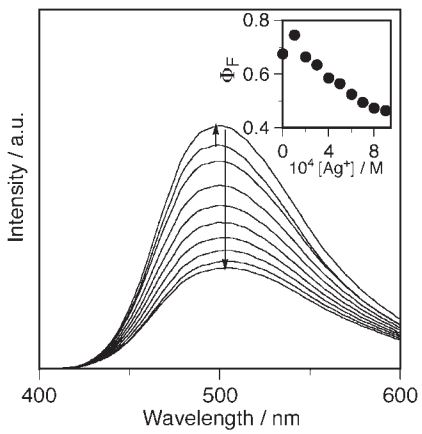
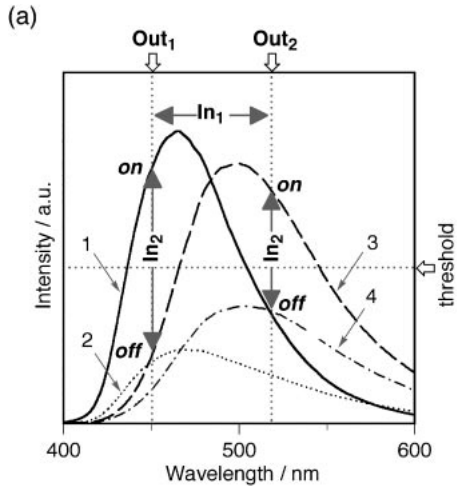


Fig. 8. Fluorescence spectra of the phthalimide **1** (1×10^{-5} M, λ_{ex} 380 nm) observed upon addition of Ag^+ (0–9×10^{-4} M) in benzene containing EtOH (250 mM). The inset shows fluorescence quantum yield of phthalimide **1** plotted as a function of [Ag^+].

Effects of Ag^+ on the green fluorescence of phthalimide **1** observed in the presence of EtOH (cf. Fig. 4) was also examined. Figure 8 shows the effects of Ag^+ on the green fluorescence of phthalimide **1**. The green emission was also quenched by Ag^+; upon addition of 90 equivalents of Ag^+, the fluorescence intensity was decreased to 41% of that observed in the absence of the additive. Therefore, Ag^+ could also switch off the fluorescence of phthalimide **1** in the presence of EtOH. Different from the case in pure benzene (Fig. 7a), the fluorescence response observed in the presence of EtOH was complex (Fig. 8, inset). The fluorescence efficiency initially increased upon addition of 10 equivalents of Ag^+, but further addition of Ag^+ resulted in a decrease of the efficiency. The observed fluorescence behavior cannot be analyzed by 1:1 complex formation between phthalimide **1** and Ag^+. This is presumably



(b)

In_1 (EtOH)	In_2 (Ag^+)	Out_1 (450 nm)	Out_2 (515 nm)
0	0	1	0
0	1	0	0
1	0	0	1
1	1	0	0

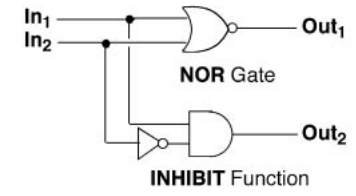


Fig. 9. (a) Fluorescence behavior of crowned phthalimide **1** in benzene (1×10^{-5} M, λ_{ex} 380 nm); curve 1: without an additive, curve 2: Ag^+ (In_2, 9×10^{-4} M), curve 3: EtOH (In_1, 250 mM), curve 4: Ag^+ and EtOH (In_1 and In_2). (b) Truth table for the fluorescence response of crowned phthalimide **1** to Ag^+ (In_2) and EtOH (In_1). 1 and 0 denote fluorescence *on* and *off*, respectively. (c) A scheme of integrated logic circuit for crowned phthalimide **1**.

because there are interactions among the three components (phthalimide **1**, Ag^+, and EtOH), which are in equilibrium under the experimental conditions; such interactions cause the observed complex fluorescence behavior.[28b]

Crowned Phthalimide 1 as a Mimic Combinational Logic Gate. Figure 9 summarizes the fluorescence response of the crowned phthalimide **1** toward EtOH (In_1) and Ag^+ (In_2) (cf. Figs. 7a and 8). Selecting wavelengths at 450 (Out_1) and 530 (Out_2) nm as output signals and setting an appropriate threshold of fluorescence intensity, one can define four states by the fluorescence spectra (curves 1–4) as illustrated in Fig. 9a, and the corresponding truth table is shown in Fig. 9b. The Out_1 is *on* without an additive (curve 1). When either EtOH (In_1) or Ag^+ (In_2) is added to phthalimide **1**, the Out_1 turns *off* (curves 2 and 3). In the presence of the both additives, the Out_1 is also *off* (curve 4). The response of Out_1 to In_1 and In_2 correspond to a NOR operation. The fluorescence output at 530 nm (Out_2) is *off* without an additive (curve 1). Upon stimulation by EtOH (In_1), the Out_2 becomes *on* (curve 3) while it turns *off* by additional input Ag^+ (In_2) (curve 4). Thus, the response of Out_2 displays an INHIBIT operation. Therefore, it is concluded that the crowned phthalimide **1** serves as a combinational logic gate of a two-input–two-output system with a single fluorophore and a single host function. A scheme of the logic circuit corresponding to the fluorescence behavior of phthalimide **1** can be drawn as shown in Fig. 9c.

By means of a flow-injection analytical system, the fluorescence response of phthalimide **1** was actually detected using a benzene solution of phthalimide **1** as a carrier solution (Fig. 10). In the absence of an input stimulus, Out_1 is *on* while Out_2 is *off*. By injection of In_1, the switching *off* of Out_1 and the switching *on* of Out_2 were simultaneously observed (Fig. 10, curves a and c). Addition of In_2 resulted in the switching *off* of Out_1 (Fig. 10, curve b). Furthermore, the Out_2, which was *on* in the presence of In_1, displayed switching *off* by injection of In_2 (Fig. 10, curve d).[42] Therefore, the integrated molecular logic gate **1** was essentially operative in such an analytical device.

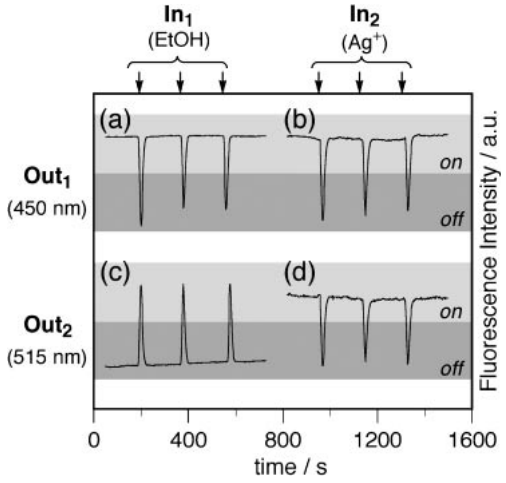


Fig. 10. Fluorescence change of phthalimide **1** (λ_{ex} 380 nm) detected by a flow-injection system using a carrier solution of **1** in benzene (1×10^{-5} M). (a), (b) Response of Out_1 (450 nm) to In_1 (EtOH, 250 mM) and to In_2 (Ag^+, 1×10^{-3} M), respectively. (c) Response of Out_2 (515 nm) to In_2 (Ag^+, 1×10^{-3} M). (d) Response of Out_2 to In_2 (Ag^+, 1×10^{-3} M) in the presence of EtOH as In_1 (250 mM).

Summary

The novel azacrowned phthalimide **1** has been prepared via the one-step crowning reaction. The crowned phthalimide **1** displayed both solvent and metal-cation sensitivity. The fluorescence color of the phthalimide can be altered by addition of EtOH (In_1) in benzene (from blue to green). Additionally, switching of the fluorescence can be achieved by stimulation with Ag^+ (In_2). By selecting the blue (450 nm, Out_1) and the green (515 nm, Out_2) fluorescence as output signals, the former and the latter outputs, respectively, displayed NOR and INHIBIT logic operation responding to the input signals (In_1 and In_2). Thus, the phthalimide **1** mimics a two-input–two-

output logic circuit with a single fluorophore and a single guest-sensing function. The present molecular design, in which a solvatofluorochromic dye is combined with a host function, provides a basis for a novel multiple-color output molecular sensing device with a simple molecular structure. Furthermore, as such a molecular sensor can simultaneously detect environmental conditions and a specific guest, the present molecular design would be applicable to construction of a fluorescent probe which is sensitive not only to a biologically important cation but also to the conditions in which the analyte exists.

Experimental

General Aspects. ^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectra were collected on a VARIAN VXR-500 spectrometer. Spectroscopic-grade solvents were used for the absorption and the fluorescence measurements as purchased. Et_2O was distilled over sodium before use. 4-Amino-*N*-methylphthalimide, pentaethylene glycol ditosylate, and 1,4-dioxane (anhydrous) were purchased from Aldrich Co., Inc. and used without further purification. 4-(Dimethylamino)-*N*-methylphthalimide **2** was prepared by *N*-methylation of 4-amino-*N*-methylphthalimide **3** with dimethyl sulfate.

Azacrowned Phthalimide 1. A suspension of 4-amino-*N*-methylphthalimide **3** (528 mg, 3 mmol) and sodium hydride (60% in oil, 360 mg, 9 mmol) in 1,4-dioxane (45 mL) was heated at 60 °C for 30 min with vigorous stirring and then cooled to room temperature. A solution of pentaethylene glycol ditosylate (1.72 g, 3.2 mmol) in 10 mL of 1,4-dioxane was added to the mixture. The resulting mixture was heated at 120 °C in a sealed glass tube for 40 h. The salts that precipitated were filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel using AcOEt as an eluent to give the crowned phthalimide **1** (228 mg, 20%). Yellow needles, mp 137–138 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, 1H, $J = 8.5$ Hz), 7.04 (d, 1H, $J = 2.5$ Hz), 6.80 (dd, 1H, $J = 8.5$, 2.5 Hz), 3.78 (t, 4H, $J = 6.2$ Hz), 3.68 (t, 4H, $J = 6.2$ Hz), 3.66–3.64 (m, 8H), 3.62 (brs, 4H), 3.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 168.8, 152.4, 135.0, 124.8, 117.8, 114.5, 105.6, 71.2, 70.3, 69.9, 67.9, 53.2, 23.7. IR (KBr) ν_{max} 1760, 1711 cm^{-1}. UV–vis (benzene) λ_{max}/nm (log ε) 315sh (3.85), 324 (3.92), 387 (3.77). HRMS (FAB) Found: 379.1803. Calcd for $C_{19}H_{27}N_2O_6$: 379.1869. Anal. Found: C, 60.68; H, 6.84; N, 7.32%. Calcd for $C_{19}H_{26}N_2O_6$: C, 60.30; H, 6.93; N, 7.40%.

Fluorescence Measurements. Fluorescence spectra were measured at 25 °C on a HITACHI F2500 spectrofluorophotometer with a 1-cm path-length quartz cell. The spectra were corrected against the instrumental response using rhodamine B. Fluorescence quantum yields were determined under aerated conditions using quinine sulfate (1×10^{-5} M) in 0.5 M sulfuric acid (Φ_F 0.55) as the reference.[43]

The flow-injection system consisted of a peristaltic pump, an HPLC sample-injection valve, and a glass flow cell which was set in a HITACHI F2500 spectrofluorophotometer. The fluorescence response was observed at 450 and 515 nm (λ_{ex} 380 nm) using a carrier solution of **1** (1×10^{-5} M) in benzene upon injection of solutions of Ag^+ (1×10^{-3} M) and EtOH (0.25 M) in the carrier solution.

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References

1 H.-G. Löhr and F. Vögtle, *Acc. Chem. Res.*, **18**, 65 (1985).
2 F. Vögtle, "Supramolecular Chemistry," Japanese translated ed, Maruzene–Wiley, Tokyo (1995).
3 a) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, and T. E. Rice, *Chem. Rev.*, **97**, 1515 (1997). b) A. P. de Silva, D. B. Fox, A. J. M. Huxley, and T. S. Moody, *Coord. Chem. Rev.*, **205**, 41 (2000).
4 a) B. Valeur and I. Leray, *Coord. Chem. Rev.*, **205**, 3 (2000). b) L. Fabbrizzi, M. Licchelli, G. Rabaioli, and A. Taglietti, *Coord. Chem. Rev.*, **205**, 85 (2000).
5 a) H. Okamoto, M. Owari, M. Kimura, and K. Satake, *Tetrahedron Lett.*, **42**, 7453 (2001). b) H. Okamoto and M. Kimura, *Luminescence*, **19**, 169 (2004).
6 "Molecular Switches," ed by B. L. Feringa, Wiley-VCH, Weinheim (2001).
7 V. Balzani, M. Venturi, and A. Credi, "Molecular Devices and Machines: A Journey into the Nanoworld," Wiley-VCH, Weinheim (2003).
8 A. Aviram, *J. Am. Chem. Soc.*, **110**, 5687 (1988).
9 M. D. Ward, *J. Chem. Educ.*, **78**, 321 (2001).
10 A. P. de Silva, H. Q. N. Gunaratne, and C. P. McCoy, *Nature*, **364**, 42 (1993).
11 a) A. P. de Silva, H. Q. N. Gunaratne, and G. E. M. Maguire, *J. Chem. Soc., Chem. Commun.*, **1994**, 1213. b) P. Ghosh, P. K. Bharadwaj, S. Mandal, and S. Ghosh, *J. Am. Chem. Soc.*, **118**, 1553 (1996).
12 A. P. de Silva, H. Q. N. Gunaratne, and C. P. McCoy, *J. Am. Chem. Soc.*, **119**, 7891 (1997).
13 A. P. de Silva, I. M. Dixon, H. Q. N. Gunaratne, T. Gunnlaugsson, P. R. S. Maxwell, and T. E. Rice, *J. Am. Chem. Soc.*, **121**, 1393 (1999).
14 a) H. T. Baytekin and E. U. Akkaya, *Org. Lett.*, **2**, 1725 (2000). b) D. Parker, *Chem. Commun.*, **1998**, 245.
15 F. Pina, M. J. Melo, M. Maestri, P. Passaniti, and V. Balzani, *J. Am. Chem. Soc.*, **122**, 4496 (2000).
16 M. Asakawa, P. R. Ashton, V. Balzani, A. Credi, G. Mattersteig, O. A. Matthews, M. Montalti, N. Spencer, J. F. Stoddart, and M. Venturi, *Chem.—Eur. J.*, **3**, 1992 (1997).
17 a) T. Gunnlaugsson, D. A. Mac Dónail, and D. Parker, *Chem. Commun.*, **2000**, 93. b) T. Gunnlaugsson, D. A. Mac Dónaill, and D. Parker, *J. Am. Chem. Soc.*, **123**, 12866 (2001).
18 A. Roque, F. Pina, S. Alves, R. Ballardini, M. Maestri, and V. Balzani, *J. Mater. Chem.*, **9**, 2265 (1999).
19 H. Xu, X. Xu, R. Dabestani, G. M. Brown, L. Fan, S. Patton, and H.-F. Ji, *J. Chem. Soc., Perkin Trans. 2*, **2002**, 636.
20 A. P. de Silva and N. D. McClenaghan, *J. Am. Chem. Soc.*, **122**, 3965 (2000).
21 J. Andréasson, G. Kodis, Y. Terazono, P. A. Liddell, S. Bandyopadhyay, R. H. Mitchell, T. A. Moore, A. L. Moore, and D. Gust, *J. Am. Chem. Soc.*, **126**, 15926 (2004).
22 a) F. M. Raymo and S. Giordani, *J. Am. Chem. Soc.*, **123**, 4651 (2001). b) S. Giordani and F. M. Raymo, *Org. Lett.*, **5**, 3559 (2003).
23 F. Pina, M. Maestri, and V. Balzani, *Chem. Commun.*, **1999**, 107.

24 L. Gobbi, P. Seiler, and F. Diederich, *Angew. Chem., Int. Ed.*, **38**, 674 (1999).

25 A. Okamoto, K. Tanaka, and I. Saito, *J. Am. Chem. Soc.*, **126**, 9458 (2004).

26 C. Reichardt, *Chem. Rev.*, **94**, 2319 (1994).

27 a) S. Nakai, M. Yasui, M. Nakazato, F. Iwasaki, S. Maki, H. Niwa, M. Ohashi, and T. Hirano, *Bull. Chem. Soc. Jpn.*, **76**, 2361 (2003). b) T. Sekiguchi, S. Maki, H. Niwa, H. Ikeda, and T. Hirano, *Tetrahedron Lett.*, **45**, 1065 (2004).

28 a) N. Marcotte, S. Fery-Forgues, and D. Lavabre, *J. Phys. Chem. A*, **103**, 3163 (1999). b) V. G. Pivovarenko, A. V. Klueva, A. O. Doroshenko, and A. P. Demchenko, *Chem. Phys. Lett.*, **325**, 389 (2000).

29 a) G. Saroja, T. Soujanya, B. Ramachandram, and A. Samanta, *J. Fluoresc.*, **8**, 405 (1998). b) R. Karmakar and A. Samanta, *J. Am. Chem. Soc.*, **123**, 3809 (2001).

30 W. Zeng, Y. Du, H. Li, X. Lu, and S. Qin, *Org. Prep. Proced. Int.*, **35**, 228 (2003).

31 J. P. Dix and F. Vögtle, *Chem. Ber.*, **113**, 457 (1980).

32 C. Reichardt, "Solvents and Solvent Effects in Organic Chemistry," 2nd ed, VCH, Weinheim (1988).

33 a) T. Soujanya, R. W. Fessenden, and A. Samanta, *J. Phys. Chem.*, **100**, 3507 (1996). b) A. Morimoito, T. Yatsuhashi, T. Shimada, L. Biczók, D. A. Tryk, and H. Inoue, *J. Phys. Chem. A*, **105**, 10488 (2001).

34 a) E. Lippert, *Z. Naturforsch.*, **10a**, 541 (1955). b) E. Lippert, *Z. Elektrochem. Angew. Phys. Chem.*, **61**, 962 (1957). c) N. Mataga, Y. Kaifu, and M. Koizumi, *Bull. Chem. Soc. Jpn.*, **28**, 690 (1955). d) N. Mataga, Y. Kaifu, and M. Koizumi, *Bull. Chem. Soc. Jpn.*, **29**, 465 (1956).

35 H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, **71**, 2703 (1949).

36 It has been reported that aza-15-crown-5 forms 1:1 complex with Ag^+ effectively: T. Ossowski, J. Kira, D. Rogowska, H. Warmke, and J. Mlodzianowski, *J. Chem. Soc., Dalton Trans.*, **2000**, 689.

37 As it has been known that Ag^+ forms complex with benzene in the ground state, strictly, the K_a determined here is equilibrium constant between (**1** + benzene·Ag^+) and (**1**·Ag^+ + benzene). However, the association of Ag^+ with benzene is very weak,[38] thus, the K_a determined here is considered to be the apparent K_a for association of crowned phthalimide **1** with Ag^+.

38 a) J. H. Lee, M. A. Schlautman, E. R. Carraway, S. Yim, and B. E. Herbert, *J. Photochem. Photobiol., A*, **163**, 165 (2004). b) L. J. Andrews and R. M. Keefer, *J. Am. Chem. Soc.*, **71**, 3644 (1949).

39 H. Masuhara, H. Shioyama, T. Saito, K. Hamada, S. Yasoshima, and N. Mataga, *J. Phys. Chem.*, **88**, 5868 (1984).

40 B. Valeur, "Molecular Fluorescence: Principals and Applications," Wiley-VCH, Weinheim (2002), pp. 77–90.

41 J. H. Lee, E. R. Carraway, M. A. Schlautman, S. Yim, and B. E. Herbert, *J. Photochem. Photobiol., A*, **167**, 141 (2004).

42 In the present flow-injection system, as the analytes passed continuously though the flow cell, the oberved *on*/*off* fluorescence signals reverted to the back-ground level immediately after the input materials run out from the detection cell.

43 W. H. Melhuish, *J. Phys. Chem.*, **65**, 229 (1961).