Control of Photophysical Properties and Photoreactions of Aromatic Imides by Use of Intermolecular Hydrogen Bonding

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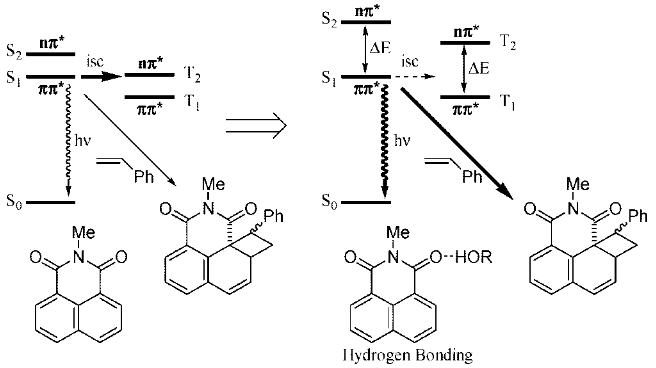

The effect of addition of alcohols on the photophysical properties and the photoreactions of *N*-methylphthalimide (**1**), *N*-methyl-1,8-, -2,3-, and -1,2-naphthalimide (**2**−**4**), and *N*-methyl-9,10-phenanthrenedicarboximide (**5**) has been investigated. The UV and IR spectra of aromatic imides **1**−**5** showed the presence of the intermolecular hydrogen bonding between the carbonyl group of the aromatic imides and the alcohols in less polar solvents. The equilibrium constants *K* for the hydrogen bonding were determined by the UV spectra. The fluorescence intensities of **2** and **1** were found to be remarkably and moderately enhanced by the addition of alcohols, respectively, though those of **3**−**5** were little enhanced by the addition of alcohols. On the other hand, photochemical cyclobutane formation of **2** with styrene (**6**) was found to be enhanced by the addition of 2,2,2-trifluoroethanol in benzene. Enhancement of the fluorescence quantum yields Φ_f and the photoreaction of **2** by the hydrogen bond formation was explained by the decrease of the efficiency of the intersystem crossing from $^1(\pi\pi^*)$ to $^3(n\pi^*)$, whose energy was increased by the hydrogen bonding.

Introduction

Hydrogen bonding in the ground state is known to play an important role in chemistry and biology.[1,2] On the other hand, the intermolecular hydrogen bond formed in the excited state has been often observed to be stronger than that in the ground state due to specific charge localization in the excited state.[3] Strong hydrogen bonds in the excited states have been reported to induce efficient radiationless deactivation, electron transfer,[4,5] and energy transfer.[6] Formation of intermolecular hydrogen bonding has been found to have a significant influence on the photophysical behavior of various compounds, in particular on that of aromatic heterocyclic[7] and carbonyl compounds.[8,9] Hydrogen bond formation had a different effect on the energies

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[1] Mellot, C. F; Davidson, A. M; Eckert, J; Cheetham, A. K. *J. Phys. Chem. B* **1998**, *102*, 2530.

[2] Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer: Berlin, 1991.

[3] Sugita, M.; Shimada, T.; Tachibana, H.; Inoue, H. *Phys. Chem. Chem. Phys.* **2001**, *3*, 2012.

[4] Miyasaka, H.; Tabata, A.; Ojima, S.; Ikeda, N.; Mataga, N. *J. Phys. Chem.* **1993**, *97*, 8222.

[5] Miyasaka, H.; Tabata, A.; Kamada, K.; Mataga, N. *J. Am. Chem. Soc.* **1993**, *115*, 7335.

[6] Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1995**, *117*, 704.

[7] Herbich, J.; Hung, C.-Y.; Thymmel, R. P.; Waluk, J. *J. Am. Chem. Soc.* **1996**, *118*, 3508, and references therein.

[8] Biczók, L.; Bérces, T.; Linschitz, H. *J. Am. Chem. Soc.* **1997**, *119*, 11071.

[9] (a) Yatsuhashi, T.; Inoue, H. *J. Phys. Chem. A* **1997**, *101*, 8166. (b) Yatsuhashi, T.; Nakayama, Y.; Shimada, T.; Tachibana, H.; Inoue, H. *J. Phys. Chem. A* **1998**, *102*, 8657, and references therein.

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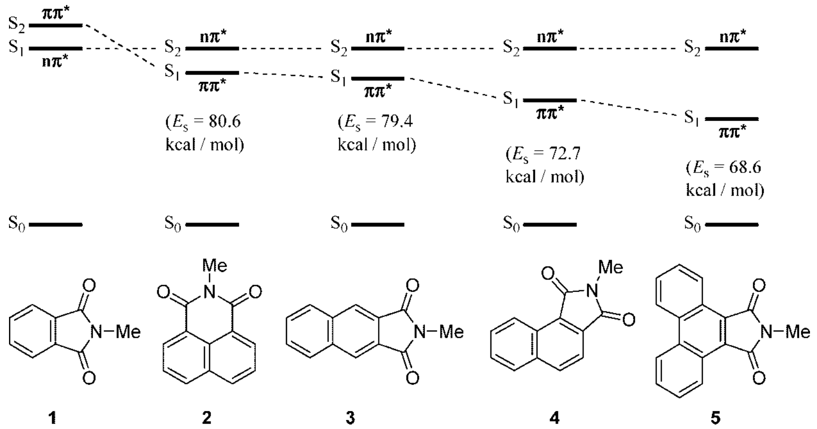
SCHEME 1



of various excited states; in an extreme case, hydrogen bonding caused the reversal of close-lying nπ* and $\pi\pi$* states.[10] In addition, the different strength of hydrogen bonding in the ground and excited states has been reported to lead to efficient energy dissipation.[8,9,11]

Derivatives of 1,8-naphthalimide have been extensively studied in recent decades owing to their interesting photophysical properties[12] and the wide range of their applications in different chemical and biochemical areas. Many naphthalimide chromophores, characterized by both strong absorption and good fluorescence yields, have been prepared in the past century and used as dyes[13] or brighteners.[14] Several 1,8-naphthalimide-containing compounds have been described as photoinducible DNA-cleaving agents[15] and tumoricidals,[16] some of them entering into clinical trials[17] owing to their strong anticancer activity. Moreover, some derivatives of 1,8-naphthalimide have been proposed as good candidates for the photochemical inhibition of enveloped viruses in blood and blood products[18] and for the fluorescent probing of hypoxic cells.[19] The 1,8-naphthalimide moiety has also been used to design fluorescent molecular probes sensitive to variations of pH[20] or metal ion concentration.[21] The photoreactions of naphthalimides have been investigated in the past decade in our laboratories.[22]

In this paper, we investigate the effect of intermolecular hydrogen bonding on the photophysics and photoreactions of aromatic imide compounds.

Results and Discussion

Five aromatic imide compounds, *N*-methylphthalimide (**1**), *N*-methyl-1,8-, -2,3-, and -1,2-naphthalimide (**2**−**4**), and *N*-methyl-9,10-phenanthrenedicarboximide (**5**), were chosen in this investigation, because of differing energies of their $\pi\pi$* and nπ* excited states (Scheme 1). The lowest singlet excited state of phthalimide **1** has been reported to be a nπ* character.[12] On the other hand, the lowest singlet excited states of naphthalimides **2**−**4** and phenanthrenedicarboximide **5** have been reported to be $\pi\pi$* characters, though the energy of the singlet states are changeable, namely, 80.6 kcal mol^{-1} for **2**, 79.4 kcal mol^{-1} for **3**, 72.7 kcal mol^{-1} for **4**, and 68.6 kcal mol^{-1} for **5**.[12] The second excited singlet states of naphthalimides **2**−**4** and phenanthrenedicarboximide **5** may have nπ* characters with a similar energy, since the nπ* excitation is localized on the carbonyl group.

Since hydrogen bonding has been known to affect the energy levels of nπ* states compared with those of $\pi\pi$* states,[23] the hydrogen bonding is anticipated to affect the different effect on the photophysical properties and the photoreactions of the aromatic imides **1**−**5**. Thus, we examined the photophysical properties and the photoreactions of the aromatic imides **1**−**5** and found the photophysical properties and the photoreactions of **2**, in which the $\pi\pi$* and nπ* levels were close in energy, were remarkably changed by the hydrogen bond formation.

Hydrogen Bonding between 2 and Alcohols in the Ground State. In order to clarify the effect of hydrogen bonding in the ground state, UV and IR spectra of **2** in the absence and in the presence of various concentrations of 2,2,2-trifluoroethanol

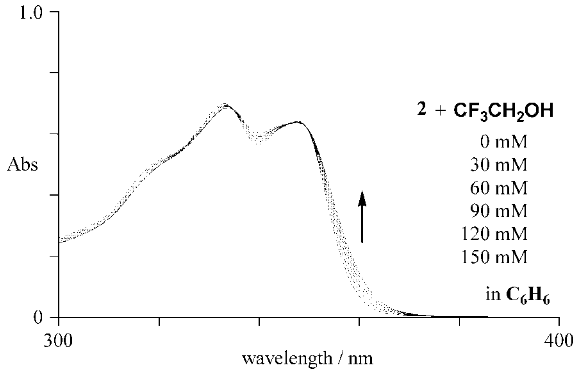


FIGURE 1. Absorption spectra of **2** (0.075 mM) with various concentrations of TFE in benzene.

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[10] va der Burgt, M. J.; Jansen, L. M. G.; Huizer, A. H.; Varma, C. A. G. O. *Chem. Phys.* **1995**, *201*, 525.

[11] (a) Sinicropi, A.; Nau, W. M.; Olivucci, M. *Photochem. Photobiol. Sci.* **2002**, *1*, 537. (b) Waluk, J. *Acc. Chem. Res.* **2003**, *36*, 832.

[12] Wintgens, V.; Valat, P.; Kossanyi, J.; Biczok, L.; Demerter, A.; Berces, T. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 411.

[13] Martin, E.; Weingand, R.; Padro, A. *J. Lumin.* **1996**, *68*, 157.

[14] Grabtchev, I.; Philipova, Tz. *Dyes Pigm.* **1995**, *27*, 321.

[15] Yao, W.; Qian, X.; Hu, Q. *Tetrahedron Lett.* **2000**, *41*, 7711.

[16] Brana, M. F.; Castellano, J. M.; Moran, M.; Perez de Vega, M. J.; Qian, X. D.; Romerdahl, C. A.; Keilhauer, G. *Eur. J. Med. Chem.* **1995**, *30*, 325.

[17] Bousquet, P. F.; Brana, M. F.; Conlon, D.; Fitzgerald, K, M.; Perron, D.; Cocchiaro, C.; Miller, R.; Moran, M.; George, J.; Qian, X. D.; Keilhauer, G.; Romerdahl, C. A. *Cancer Res.* **1995**, *55*, 1176.

[18] Chanh, C. T.; Lewis, D. E.; Judy, M. M.; Sogandares- Bernal, F.; Michalek, G. R.; Utecht, R. E.; Skiles, H.; Chang, S. C.; Matthews, J. L. *Antiviral Res.* **1994**, *25*, 133.

[19] Middleton, R. W.; Parrick, J. *J. Heterocycl. Chem* **1985**, *22*, 1567.

[20] Duffy, L. M.; de Silva, A. P.; Gunaratne, H. Q. N.; Huber, C.; Lynch, P. L. M.; Werner, T.; Wolfbeis, O. *Chem. Eur. J.* **1998**, *4*, 1810.

[21] Ramachandram, B.; Saroja, G.; Sankaran, N. B.; Samanta, A. *J. Phys. Chem. B* **2000**, *104*, 11824.

[22] Kubo, Y.; Suto, M.; Tojo, S.; Araki, T. *J. Chem. Soc., Perkin Trans. 1* **1986**, 771.

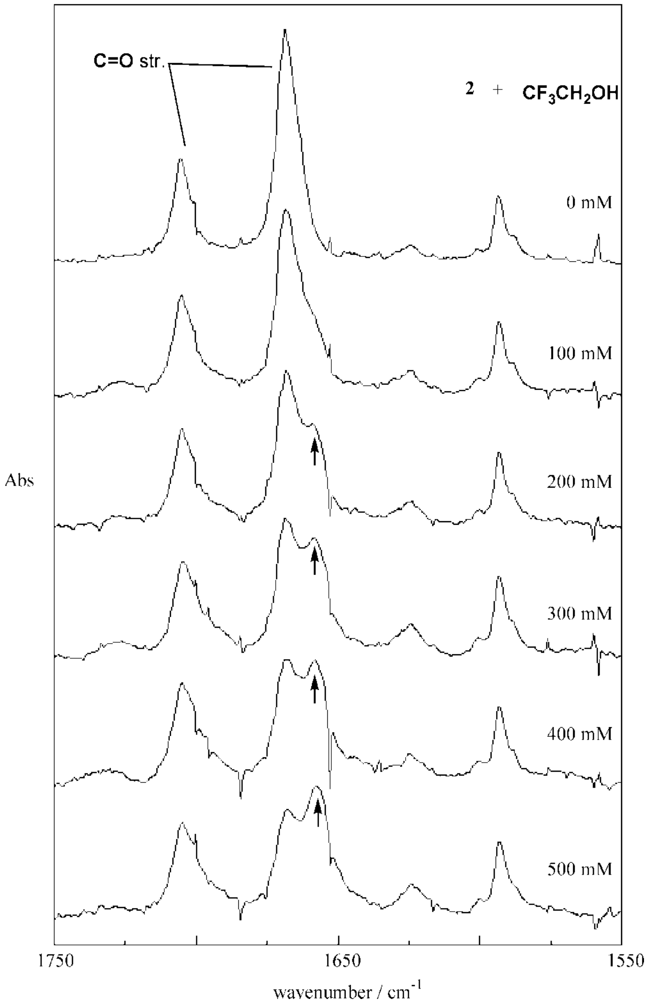


FIGURE 2. IR spectra of the ν C=O region of **2** (20 mM) with various concentrations of TFE in benzene.

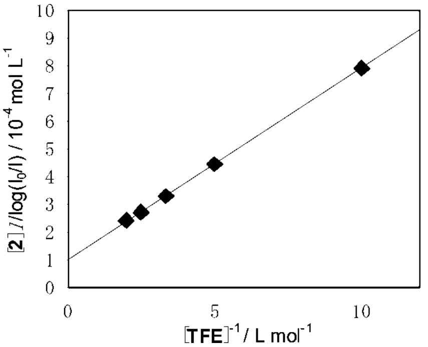


FIGURE 3. Benesi–Hildebrand plot for the hydrogen bonding of **2** and TFE in benzene.

(TFE) were measured in benzene (Figures 1 and 2). Figure 1 shows the red shift of the absorption of **2** by the addition of TFE, and Figure 2 shows the decrease of the intensity of the 1669 cm^{-1} band attributed to ν C=O of **2** and the simultaneous increase of a new 1657 cm^{-1} band attributed to ν C=O of hydrogen bonded species by the addition of TFE. The ν C=O bands of carbonyl compounds have been reported to be very sensitive to changes in the chemical environment. Thus, the results shown in Figures 1 and 2 clearly indicate the formation of hydrogen bonding between the carbonyl group of **2** and TFE in the ground state.

TABLE 1. **Association Constant *K* for Hydrogen Bonding of Imides 1–5 and Alcohols**

			K	
imide	alcohol	α^a	C_6H_6	CH_2Cl_2
1	CF_3CH_2OH	1.51	1.3	
2	CF_3CH_2OH	1.51	1.5	1.5
	$(CF_3)_2CHOH$	1.96		3.1
	$(CH_3)_2CHCH_2OH$	0.79		0.34
3	CF_3CH_2OH	1.51	2.3	
4	CF_3CH_2OH	1.51	0.90	
5	CF_3CH_2OH	1.51	0.93	

[a] Hydrogen bond donation ability.

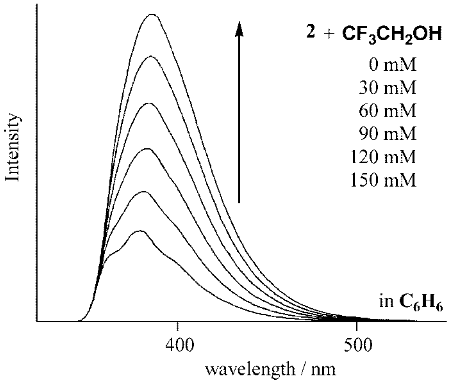
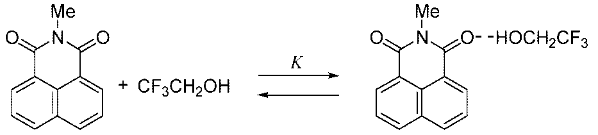


FIGURE 4. Fluorescence spectra of **2** (0.075 mM) with various concentrations of TFE in benzene.

The presence of an isosbestic point at 335 nm in Figure 1 suggests the 1:1 complex formation as shown in eq 1, and the association constant *K* in benzene is determined to be 1.5 M^{-1} from a linear Benesi–Hildebrand plot using the absorbance at 360 nm (Figure 3 and eq 2).



2

(1)

$$[\mathrm{Im}]l/\mathrm{Abs} = 1/K\varepsilon(1/[\mathrm{Alc}]) + 1/\varepsilon \qquad (2)$$

Here, [Im] and [Alc] are the concentrations of imide and alcohol, respectively, l is optical path length, ε is molar extinction coefficient of the complex, and K is the association constant.

In a similar way, association constants *K* of hydrogen bonding of **2** and TFE, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), and 2-methyl-1-propanol in dichloromethane were determined to be 1.5, 3.1, and 0.34 M^{-1}, respectively (Table 1). The association constants *K* show a reasonable correlation to the hydrogen bond donation ability[24] α of the alcohols as shown in Table 1.

Effect of Hydrogen Bonding on Fluorescence Spectra of 2. In order to clarify the effect of hydrogen bonding in the excited singlet state, fluorescence spectra of **2** in the absence and in the presence of various concentrations of TFE were measured in benzene (Figure 4). Figure 4 shows the remarkable increase of the fluorescence intensity by the addition of TFE. In a similar way, effect of the addition of TFE, HFIP, and 2-methyl-1-propanol on the fluorescence quantum yields Φ_f of **2** in dichloromethane were determined, and the results are shown in Figure 5. Reasonable correlation was observed between the

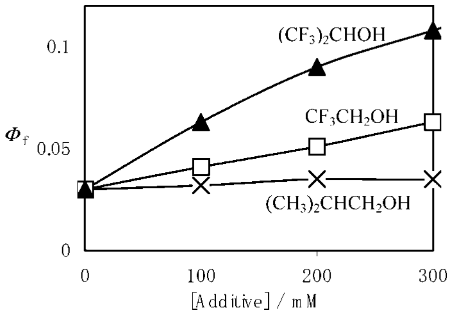


FIGURE 5. Effect of addition of alcohols on the fluorescence quantum yieldΦ_f of **2** in CH_2Cl_2.

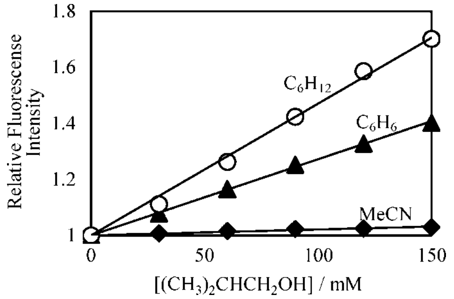


FIGURE 6. Relative fluorescence of **2** with various concentrations of $(CH_3)_2CHCH_2OH$.

degree of enhancement of Φ_f and the hydrogen bond donation ability α of the alcohols as shown in Table 1.

Figure 6 shows the solvent effect on the enhancement of the fluorescence of **2** by the addition of 2-methyl-1-propanol. In polar solvent such as acetonitrile, the fluorescence of **2** was little enhanced by the addition of 2-methyl-1-propanol. On the contrary, in nonpolar solvent such as cyclohexane, fluorescence of **2** was remarkably enhanced by the addition of 2-methyl-1-propanol. In less-polar solvent such as benzene, the degree of enhancement of fluorescence of **2** by the addition of 2-methyl-1-propanol took a position between that in acetonitrile and that in cyclohexane. The solvent effect may be explained by the disruption of hydrogen bonding between the carbonyl group of **2** and the alcohols by the polar solvents.

Effect of Hydrogen Bonding on UV and Fluorescence Spectra of Other Aromatic Imides. The effect of the addition of TFE on the absorption spectra of aromatic imides **1**, **3**, **4**, and **5** in benzene are shown in Figures S1−S4 in Supporting Information. Furthermore, the association constants *K* between aromatic imide compounds and TFE were also determined from Benesi−Hildebrand plots and are shown in Table 1. Table 1 shows that the *K* values of imides **1**, **3**, **4**, and **5** are comparable to that of **2**.

The effect of the addition of TFE on the fluorescence spectra of aromatic imides **1**, **3**, **4**, and **5** in benzene are shown in Figures 7–10, which indicate that the fluorescence of **1** is enhanced by the addition of TFE in benzene, while the fluorescence of **3**, **4**, and **5** is not enhanced by the addition of TFE. Figure 11 shows that the effect of addition of TFE on the relative fluorescence intensity of aromatic imide compounds **1**−**5** in benzene. The remarkable effect was observed for **1** and **2**, in which the $\pi\pi^*$ and $n\pi^*$ levels were close in energy, the fluorescence of **2** in the presence of 500 mM of TFE was enhanced by a factor of >10 compared with that in the absence of TFE, and the fluorescence of **1** was also moderately enhanced in the presence of TFE.

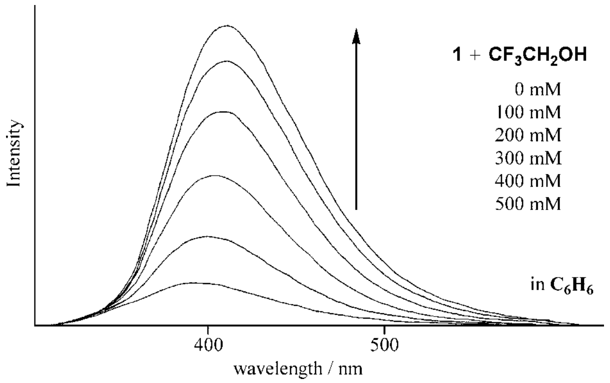


FIGURE 7. Fluorescence spectra of **1** (0.30 mM) with various concentrations of TFE in benzene.

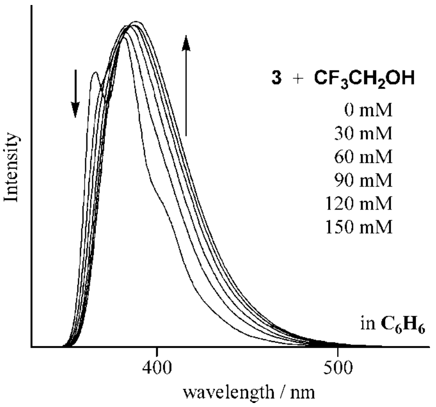


FIGURE 8. Fluorescence spectra of **3** (0.18 mM) with various concentrations of TFE in benzene.

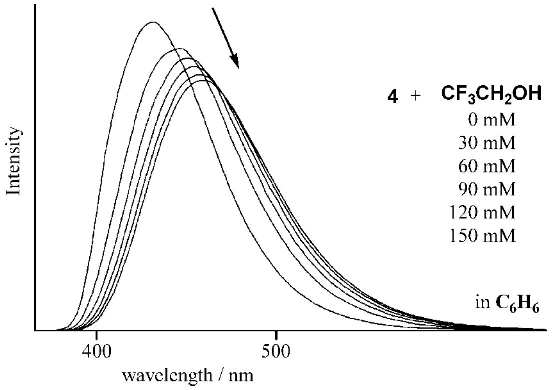


FIGURE 9. Fluorescence spectra of **4** (0.26 mM) with various concentrations of TFE in benzene.

Effect of Hydrogen Bonding on Photoreaction of 2 with Styrene. In order to clarify the effect of hydrogen bonding on the photoreactions of aromatic imide compounds, photoreactions of **2** and styrene (**6**) in benzene were examined in the absence of TFE and in the presence of 150 mM TFE, and the results are shown in Table 2. In the photoreactions of **2** and **6**, two regioisomers of cyclobutanes, **7** and **8**, were formed from the reaction of the singlet excited state of **2** with **6**, and **7** and **8** were decomposed to starting materials **2** and **6** upon prolonged irradiation (Scheme 2).[23] Table 2 shows that the hydrogen bonding by TFE accelerates the photoreaction of **2** as well as the fluorescence quantum yield.

Mechanism To Account for the Effect of the Introduction of the Hydrogen Bonding. Wintgens et al. have reported that

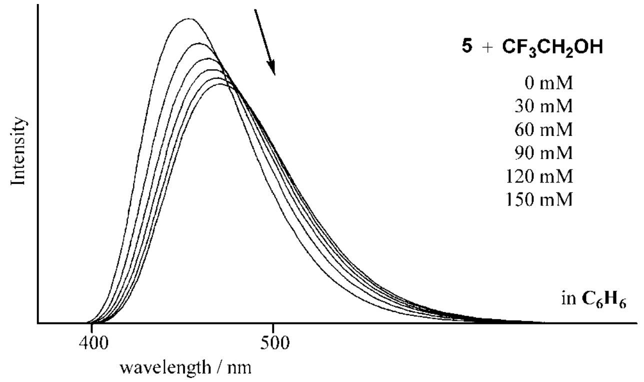


FIGURE 10. Fluorescence spectra of **5** (0.14 mM) with various concentrations of TFE in benzene.

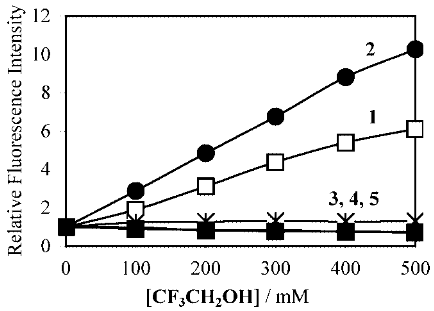


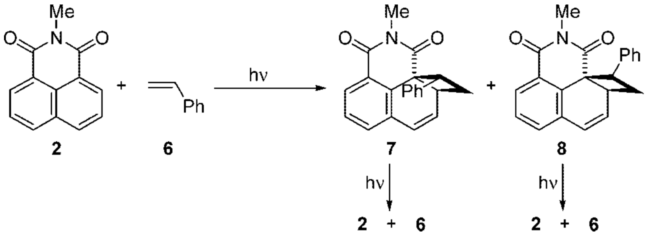
FIGURE 11. Relative fluorescence of aromatic imides **1**−**5** with various concentrations of TFE in benzene.

TABLE 2. Yield of Adducts 7 and 8 in Photoreactions of 2 and 6 in the Absence and Presence of TFE[a]

			yield[b] (%)	
additive	irradiation time (min)	conversion (%)	7	8
none	10	19	38	41
	30	27	24	54
	60	35	19	44
	120	48	15	36
TFE(CF_3CH_2OH, 150 mM)	10	58	51	36
	30	66	37	34
	60	72	24	24
	120	73	21	18

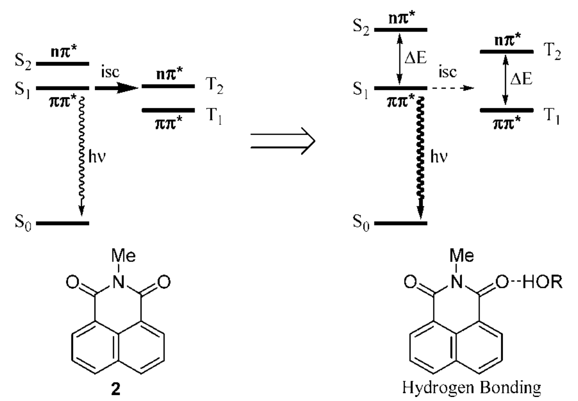
[a] [**2**] = 2.0 mM. Irradiation was carried out at room temperature, in benzene. [b] Yield was based on consumed **2**.

SCHEME 2



the rate of the intersystem crossing from the singlet excited state of **2** to the triplet state is faster than those of other naphthalimides **3** and **4**, and the intersystem crossing of **2** accounts for >90% of the deactivation processes of the singlet excited state of **2**.[12] The results may indicate that the $^1(\pi\pi^*)$ and $^3(n\pi^*)$ levels of **2** are close in energy.

SCHEME 3



As mentioned above, fluorescence quantum yield Φ_f of **2** and photoreactivity of **2** with **6** in benzene was remarkably enhanced by the introduction of the intermolecular hydrogen bonding by TFE. As the $^1(\pi\pi^*)$ and $^3(n\pi^*)$ levels of **2** are close in energy and the hydrogen bond formation is known to increase the energy of $n\pi^*$ states compared with those of $\pi\pi^*$ states, the hydrogen bond formation to **2** may increase the energy of the $^3(n\pi^*)$ of **2** compared with that of $^1(\pi\pi^*)$, decrease the rate of the intersystem crossing from the $^1(\pi\pi^*)$ to the $^3(n\pi^*)$ of **2**, and thus increase the fluorescence quantum yield Φ_f and photoreactivity of the singlet excited state of **2** (Scheme 3).

Conclusions

Our results show that the hydrogen bonding of aromatic imides **1** and **2** with alcohols, such as TFE, in the ground state decreases the rate of the intersystem crossing from the $^1(\pi\pi^*)$ to the $^3(n\pi^*)$, whose energy is selectively increased by the hydrogen bonding, and thus increases the fluorescence quantum yield Φ_f and photoreactivity of the singlet excited state of **2**. It may be interesting that the simple addition of alcohol can markedly control the photophysical properties and the photoreactivity of aromatic imides widely used in numerous applications.

Experimental Section

Fluorescence quantum yields were determined relative to that of *N*-methyl-1,8-naphthalimide (**2**) in MeCN ($\Phi_f = 0.027$).

Materials. The preparation, purification, and charactarization of imide compounds **1**,[25] **2**,[26] **3**,[27] **4**,[12] and **5**[28] have been described elsewhere. Solvents, alcohols and styrene (**6**) were commercially available.

Supporting Information Available: Figures S1−S4 showing the changes in UV spectra of **1** and **3**−**5** in the presence of various concentrations of TFE in benzene. This material is available free of charge via the Internet at http://pubs.acs.org.

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(23) Brealey, G. J.; Kasha, M. *J. Am. Chem. Soc.* **1955**, *77*, 4462.
(24) Marcus, Y. *Chem. Soc. Rev* **1993**, *6*, 409.
(25) Sachs, F. *Chem. Ber* **1898**, *31*, 1228.
(26) Somich, C.; Mazzocchi, P. H.; Ammon, H. L. *J. Org. Chem.* **1987**, *52*, 3614.
(27) Kubo, Y.; Suto, M.; Araki, T. *J. Org. Chem.* **1986**, *51*, 4404.
(28) Kubo, Y.; Asai, N.; Araki, T. *J. Org. Chem.* **1985**, *50*, 5484.