

Control of Photophysical Properties of 1,8-Naphthalimides by Electron-Withdrawing Substituents Introduced into *N*-Alkyl Side Chains

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The fluorescence intensity of naphthalimides **1**–**7** in dichloromethane was found to be remarkably enhanced by the introduction of an electron-withdrawing substituent, such as OCOMe, CO_2Me, Cl, and CN, into the *N*-alkyl side chain. The rate constants of the fluorescence emission k_f, the intersystem crossing k_{isc}, and the internal conversion k_{ic} for **1**–**7** in dichloromethane and in acetonitrile were determined based on the measurements of the fluorescence lifetimes τ_f, by using picosecond single photon counting, and the quantum yields of the intersystem crossing Φ_{isc} determined by time-resolved thermal lensing. These results indicate that the value of k_{isc} decreases with an increase in the electron-withdrawing ability of the substituent. Furthermore, an almost linear Hammett relationship ($\rho = -1.48$ in dichloromethane, $\rho = -1.85$ in acetonitrile) between the logarithm of k_{isc} and the substituent constant σ_I for inductive effect of the substituent through the σ bond was observed. The enhancement of the fluorescence intensity by the introduction of electron-withdrawing substituents was thus explained by a decrease in the efficiency of the intersystem crossing from $^1(\pi\pi^*)$ to $^3(n\pi^*)$, whose energy was increased by the inductive effect of the substituent through the σ bonds.

Naphthalimides are known to be promising anticancer agents, showing broad-spectrum activity against a variety of human solid tumor cells.[1] Some naphthalimides have reached the phase of clinical trials.[2] Their DNA binding or enzyme inhibitory activity is believed to be pivotal in exerting antitumor effects. The dicationic compounds have proven to be more potent than the monocationic analogs.[3] 1,8-Naphthalimide derivatives with intramolecular dialkylammonium moieties exhibit much stronger association to oligodeoxynucleotides than the corresponding neutral molecules due to electrostatic interactions with the phosphate groups.[4]

Photoinduced processes of naphthalimides are also of particular interest because of their broad-ranging applications in fundamental studies and advanced technology as well as in biological and medical areas. Naphthalimides are capable of initiating the photocleavage of DNA[5] and photochemical crosslinking of proteins.[6] Irradiation of their brominated derivatives with visible light has been shown to generate photoproducts with strong antiviral activity.[7]

Additionally, investigations of the photophysical behavior of naphthalimides have contributed to the development of new fluorescent probes[8] and optical sensors.[9] The marked changes of the fluorescence intensity and maximum of 6-(*N*,*N*-dimethylamino)-2,3-naphthalimide corresponding to the changes of the microenvironment can be implemented for monitoring protein–protein interactions.[10] Dual fluorescence has been reported for several substituted *N*-phenylnaphthalimides[11] and the relative intensity of the two fluorescence bands has been shown to be sensitive to solvent polarity, temperature,[12] viscosity,[13] and pressure.[14]

The photoreactions of naphthalimides have been investigated over the past decade by Kubo and co-workers.[15] Matsubayashi and Kubo have recently shown that the fluorescence intensity and photoreactivity of *N*-methyl-1,8-naphthalimide (**1**) are remarkably increased by intermolecular hydrogen bonding with alcohols.[16] Furthermore, Kubo and co-workers have reported that intramolecular hydrogen bond formation in 1,8-naphthalimide derivatives decreases the rate of intersystem crossing from $^1(\pi\pi^*)$ to $^3(n\pi^*)$, that results from an increase in the energy of the $^3(n\pi^*)$ level due to the presence of the hydrogen bonding, while the rates of fluorescence emission and internal conversion were minimally affected.[17] In the course of our investigations, we have found that the introduction of electron-withdrawing substituents into the *N*-methyl group of **1** gave rise to a surprising enhancement in the fluorescence intensities. In this paper, we present our systematic investigation on the effect of the introduction of electron-withdrawing substituents, such as OCOMe, CO_2Me, Cl, and CN, into the *N*-alkyl side chains on the photophysical properties of 1,8-naphthalimides **1**–**7** (Chart 1).

Results and Discussion

UV Spectra. To clarify the effect of the introduction of electron-withdrawing substituents into the *N*-alkyl side chain of 1,8-naphthalimides in the ground state, UV spectra of **1**–**7** were measured in dichloromethane (Figure 1). Figure 1 shows the slight red shift of the absorption spectra with an increase of the electron-withdrawing ability of the substituents.

Fluorescence Spectra. To clarify the effect of the introduction of electron-withdrawing substituents into the *N*-

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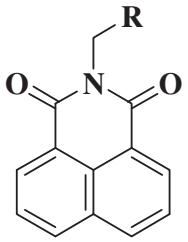


1 ; R = H
2 ; R = $(CH_2)_2OCOMe$
3 ; R = CH_2OCOMe
4 ; R = OCOMe
5 ; R = CO_2Me
6 ; R = Cl
7 ; R = CN

Chart 1.

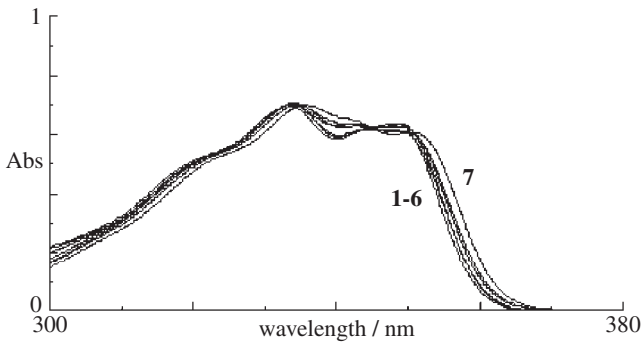


Figure 1. Absorption spectra of naphthalimides **1**–**7** (0.060 mM) in dichloromethane.

alkyl side chain of 1,8-naphthalimides in the singlet excited state, fluorescence spectra of **1**–**7** were measured in dichloromethane. The spectra of **1** and **4**–**7**, and **1**–**4** are shown in Figures 2 and 3, respectively. Figure 2 shows that the fluorescence intensity of **1** (R = H, Chart 1), **4** (R = OCOMe), **5** (R = CO_2Me), **6** (R = Cl), and **7** (R = CN) increases with an increase in the electron-withdrawing ability of the substituent introduced into the *N*-methyl group of **1**. Figure 3 shows that the fluorescence intensity of **1** (R = H, Chart 1), **2** [R = $(CH_2)_2$OCOMe], **3** (R = CH_2OCOMe), and **4** (R = OCOMe) decreases as the number of methylene groups between the imide and the electron-withdrawing OCOMe group increases, indicating that the effect of the electron-withdrawing substituent introduced into the *N*-alkyl side chains on the fluorescence intensity is caused by the inductive effect of the substituent through σ bonds.

Photophysical Properties. The fluorescence lifetimes τ_f of **1**–**7** in aerated dichloromethane and acetonitrile at 293 K were measured by picosecond single photon counting. The fluorescence quantum yields Φ_f of **1**–**7** in aerated dichloromethane and acetonitrile were determined as relative values to that of **1** in acetonitrile ($\Phi_f = 0.027$).[18] It should be emphasized here that the enhancement of the fluorescence intensity by the introduction of the electron-withdrawing substituent occurred even in polar acetonitrile as well in less polar dichloromethane, while

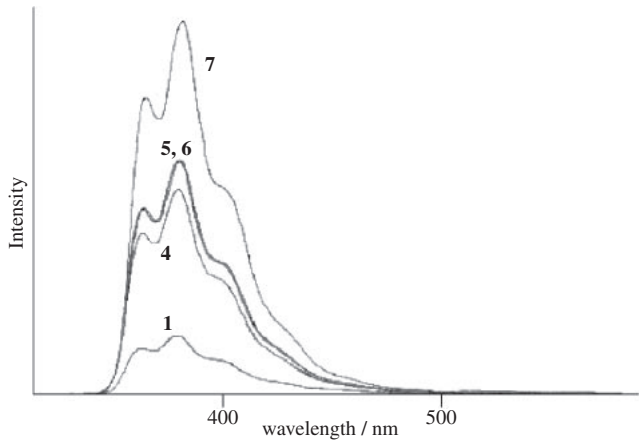


Figure 2. Fluorescence spectra of naphthalimides **1** and **4**–**7** (0.060 mM) in dichloromethane with an excitation wavelength of 333 nm.

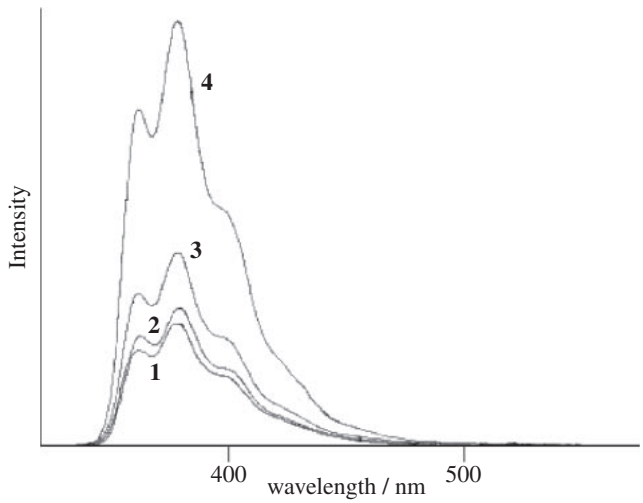


Figure 3. Fluorescence spectra of naphthalimides **1**–**4** (0.060 mM) in dichloromethane with an excitation wavelength of 333 nm.

the enhancement of the fluorescence intensity by hydrogen bond formation was observed only in nonpolar and less polar solvents.[16]

The quantum yields of the intersystem crossing Φ_{isc} of **1**–**7** in aerated dichloromethane and acetonitrile at 293 K were determined by using time-resolved thermal lensing (TRTL).[19] The quantum yields of the internal conversion Φ_{ic} were derived using the following equation:

$$\Phi_{ic} = 1 - \Phi_f - \Phi_{isc} \quad (1)$$

The rate constants of the fluorescence emission k_f, the intersystem crossing k_{isc}, and the internal conversion k_{ic} were calculated from the equations given below:

$$k_f = \Phi_f \tau_f^{-1} \quad (2)$$

$$k_{isc} = \Phi_{isc} \tau_f^{-1} \quad (3)$$

$$k_{ic} = \Phi_{ic} \tau_f^{-1} \quad (4)$$

The photophysical parameters of **1**–**7** in dichloromethane and acetonitrile are summarized in Table 1. The data show that

Table 1. Photophysical Parameters for Naphthalimides **1**–**7**

Solvent	Imide	τ_f/ps	Φ_f	Φ_{isc}[a)]	Φ_{ic}	$k_f/10^8\,s^{-1}$	$k_{isc}/10^9\,s^{-1}$	$k_{ic}/10^8\,s^{-1}$	σ_I[b)]
CH_2Cl_2	**1**	180	0.030	0.92	0.05	1.7	5.1	2.8	0
	2	218	0.033	0.91	0.06	1.5	4.2	2.8	0.05
	3	292	0.046	0.89	0.06	1.6	3.0	2.1	0.14
	4	620	0.104	0.84	0.06	1.6	1.4	0.97	0.39
	5	688	0.110	0.85	0.04	1.6	1.2	0.58	0.30[c)]
	6	716	0.111	0.83	0.06	1.6	1.2	0.84	0.47
	7	1010	0.180	0.77	0.05	1.8	0.78	0.50	0.58
MeCN	**1**	177	0.027	0.92	0.05	1.5	5.2	2.8	0
	2	205	0.033	0.91	0.06	1.6	4.4	2.9	0.05
	3	303	0.047	0.89	0.06	1.6	2.9	2.0	0.14
	4	797	0.110	0.83	0.06	1.4	1.0	0.75	0.39
	5	863	0.140	0.79	0.07	1.6	0.92	0.81	0.30[c)]
	6	952	0.145	0.80	0.06	1.5	0.84	0.63	0.47
	7	1450	0.230	0.70	0.07	1.6	0.48	0.48	0.58

a) The Φ_{isc} values were determined using TRTL. b) The substituent constants σ_I for the inductive effect through σ bonds for the substituents R shown in Chart 1. c) The σ_I values for CO_2R.

the values of k_{isc} ($\approx 10^9\,s^{-1}$) are significantly larger than those of k_f ($\approx 10^8\,s^{-1}$) and k_{ic} ($\approx 10^8\,s^{-1}$) for **1**–**7** in both dichloromethane and acetonitrile, indicating that the intersystem crossing is the most dominant relaxation process ($\Phi_{isc} > 0.70$) from the lowest singlet excited state $^1(\pi\pi^*)$ of **1**–**7**. Furthermore, these results indicate that the introduction of electron-withdrawing substituents into the *N*-alkyl side chains mainly affects the rate constant of the intersystem crossing k_{isc}, and the values of k_{isc} remarkably decrease with an increase of the electron-withdrawing ability of the substituent.

Hammett Relationship. To evaluate the inductive effect of the substituents introduced into the *N*-methyl group of *N*-methyl-1,8-naphthalimide (**1**), the Hammett relationship was applied:

$$\log(k_{isc}/k_{iscH}) = \rho\sigma_I \quad (5)$$

An almost linear Hammett relationship ($\rho = -1.48$ in dichloromethane, $\rho = -1.85$ in acetonitrile) between the logarithm of k_{isc} for **1**–**7** and the substituent constant σ_I[20] for the inductive effect through σ bonds for the substituents R shown in Chart 1 was observed. Some deviations were observed for **5**, possibly due to the uncertainty of the substituent constant σ_I for CO_2Me (Figure 4). These results suggest that a considerable positive charge is developed on the nitrogen atom of naphthalimides **1**–**7** in the course of the intersystem crossing from the lowest singlet excited state $^1(\pi\pi^*)$ to the upper triplet excited state $^3(n\pi^*)$, whose n and π^* orbital localize mainly in the imide moiety and in the naphthalene ring, respectively (Scheme 1).

Mechanism. Wintgens et al. have reported that the $^1(\pi\pi^*)$ and $^3(n\pi^*)$ levels of **1** are close together in energy.[18] The present investigation reveals that the intersystem crossing from $^1(\pi\pi^*)$ to $^3(n\pi^*)$ is the most important deactivation process of the singlet excited state of **1**–**7** and the value of k_{isc} remarkably decreases with an increase of the electron-withdrawing ability of the substituent introduced into the *N*-alkyl side chains. The introduction of the electron-withdrawing substituent may increase the energy of the upper triplet excited state $^3(n\pi^*)$ state relative to that of the lowest singlet excited state $^1(\pi\pi^*)$ by the inductive effect of the substituents through σ bonds since a considerable positive charge is developed on the nitrogen atom in the triplet excited state $^3(n\pi^*)$. The value of k_{isc} from the $^1(\pi\pi^*)$ to the $^3(n\pi^*)$ state was thus decreased because of an increasing energy gap between the $^1(\pi\pi^*)$ and the $^3(n\pi^*)$ (Scheme 2).

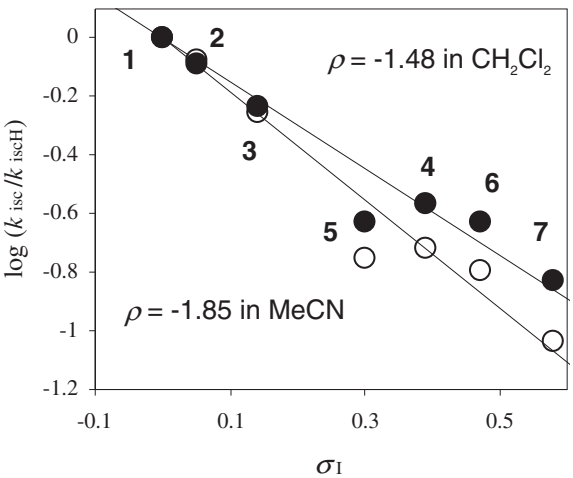
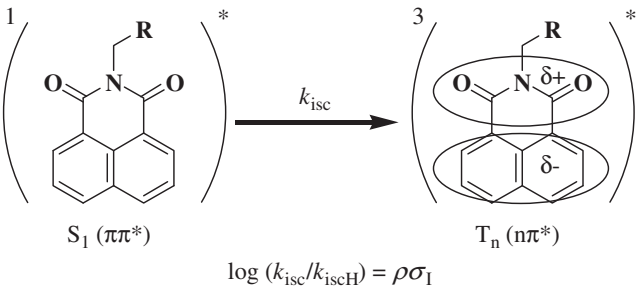
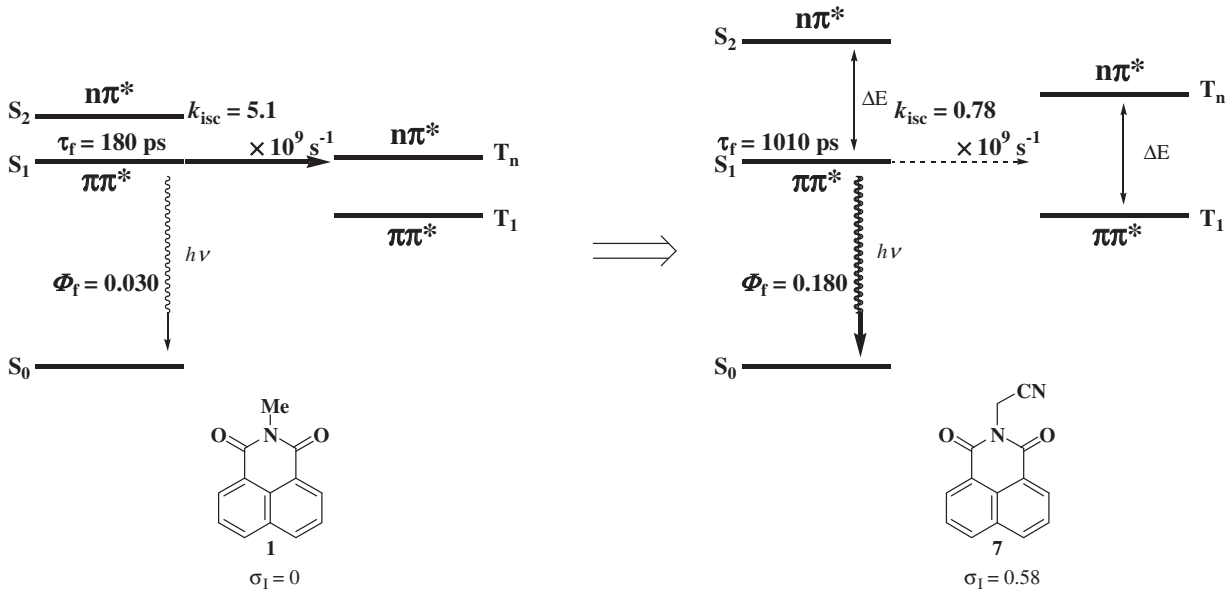


Figure 4. Hammett plot for the rate constants of the intersystem crossing k_{isc} in dichloromethane (●) and acetonitrile (○) versus substitution constant σ_I for naphthalimides **1**–**7**.



Scheme 1.



Scheme 2.

Conclusion

The photophysical properties and the excited-state reactivity of 1,8-naphthalimide derivatives have been widely studied by Kossanyi and co-workers,[13] Pardo et al.,[21] Brown and co-workers,[22] Samanta et al.,[23] and others.[5c,11d,24] However, to our knowledge there has been little systematic information on the inductive (nonresonance) effect of the substituents through σ bonds. It is interesting that the simple introduction of an electron-withdrawing group into the *N*-alkyl side chain can markedly control the photophysical properties of 1,8-naphthalimide derivatives used in numerous applications.

We have found that the fluorescence intensity of **1** is remarkably increased by hydrogen bond formation with alcohols.[16,17] While the effect of the hydrogen bond formation with alcohols has some resemblance to the effect of the introduction of the electron-withdrawing substituent into the *N*-alkyl side chain, the effect of the introduction of the substituent has advantages in that additives such as alcohols are not required, and that these derivatives will work even in polar solvents, such as acetonitrile.

Experimental

General. UV spectra were measured at ambient temperature under aerated conditions by use of a JASCO UVIDEC-650 spectrometer. Fluorescence spectra were obtained at ambient temperature under aerated conditions on a Hitachi 850 spectrophotometer. Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. NMR spectra were recorded on a JEOL JNM-AL-400 (400 MHz) instrument. Chemical shifts are reported in ppm (δ) relative to an internal standard ($SiMe_4$). IR spectra were obtained using a JASCO FT/IR-350 spectrometer. Mass spectra (EI, 70 eV) were recorded on a Hitachi M-80B mass spectrometer. Combustion analyses were performed on a Yanagimoto CHN corder MT-5.

The picosecond lifetime measurements were carried out by using a self-mode-locked Ti:sapphire laser (center wavelength: 800 nm, pulse width: ca. 70 fs, repetition rate: 82 MHz) pumped by a Nd^{3+}:YAG laser (532 nm, 4.5 W). The generation of the second harmonic (400 nm, pulse width: ca. 200 fs) was performed in a lithium triborate (LBO) crystal. The third harmonic (266 nm, pulse width: ca. 250 fs) was generated by a sum frequency mixing of the fundamental and the second harmonic. The repetition frequency of the excitation pulse was reduced to 4 MHz by using a pulse picker. The second harmonic (400 nm) in the output beam was used as trigger pulse. The fluorescence from the sample solution was observed through a polarizer at the magic angle (54.7°) with respect to the polarization direction of the excitation laser pulse. The emission light was detected by a microchannel plate after passing through a monochromator. The instrument response function had a half-width of 20–25 ps. Analysis of the fluorescence decay curves was carried out using deconvolution. The picosecond lifetime measurements were carried out at 293 K under aerated conditions.

The quantum yields for intersystem crossing (Φ_{isc}) in naphthalimides were determined by means of time-resolved thermal lensing (TRTL). For TRTL measurements, the third harmonic (355 nm) of a nanosecond Nd^{3+}:YAG laser (pulse width: 6 ns) was utilized for the excitation source. A He-Ne laser beam (633 nm) was used as the monitoring light. The probe light was introduced into a monochromator after passing through an optical filter and a small pinhole (300 μm diameter). The intensity change of the probe beam was detected by a photomultiplier. The TRTL signals were recorded on a digitizing oscilloscope and were averaged over five hundred laser shots to improve the signal-to-noise ratio. The absorbance of the sample solutions for the TRTL measurements was adjusted to ca. 0.10 at the excitation wavelength. The TRTL experiments were carried out at 293 K under aerated conditions.

The quantum yields of the intersystem crossing Φ_{isc} of **1**–**7** are given by:

$$\frac{U_{slow}}{U_{total}} = \frac{\Phi_{isc} E_T}{E_{ex} - \Phi_f \langle E_s \rangle} \quad (6)$$

where U_{slow}/U_{total}, E_T, E_{ex}, and $\langle E_s \rangle$ are the ratio of the intensity of the slow rise component (U_{slow}) and that of the total TRTL signal (U_{total}), the 0–0 transition energy of ^{3}**1**–**7***, the excitation photon energy (80.5 kcal mol^{-1}, 28170 cm^{-1}), and the average energy dissipated by fluorescence from ^{1}**1**–**7***, respectively. The E_T values of **1**, **2**, **3**, **4**, **5**, **6**, and **7** were determined to be 52.9, 52.9, 52.8, 53.0, 52.9, 53.1, and 53.0 kcal mol^{-1} from the 0–0 bands of the phosphorescence spectra of **1**, **2**, **3**, **4**, **5**, **6**, and **7** in EPA at 77 K, and the $\langle E_s \rangle$ values of **1**, **2**, **3**, **4**, **5**, **6**, and **7** were determined to be 75.64, 75.44, 75.44, 75.44, 75.44, 75.24, and 75.04 kcal mol^{-1} in dichloromethane from the wavelength of the maximum intensity of the fluorescence of **1**–**7** and to be 76.04, 76.04, 76.04, 75.44, 75.44, 75.24, and 75.24 kcal mol^{-1} in acetonitrile, respectively.

The values of Φ_{isc} were reproducible to about ±1–2% on repeated measurements.

Materials. *N*-Methyl-1,8-naphthalimide (**1**) was prepared according to a published procedure.[25]

***N*-(3-Acetyloxypropyl)-1,8-naphthalimide (2):** A mixture of *N*-(3-hydroxypropyl)-1,8-naphthalimide (1.0 g, 3.9 mmol),[17] acetic anhydride (0.80 mL), and sulfuric acid (5.0 mL) was heated until it dissolved. After cooling, the solution was poured into 100 mL of 5% sodium carbonate aqueous solution and the precipitate was filtered. The crude product was purified by chromatography and recrystallized from methanol. The yield of **2** was 0.23 g (0.77 mmol, 21%). Mp 95.8–96.5 °C. ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 3H), 2.10 (m, 2H), 4.19 (t, $J = 6.7$ Hz, 2H), 4.31 (t, $J = 6.7$ Hz, 2H), 7.76 (dd, $J = 7.3$, 8.1 Hz, 2H), 8.22 (d, $J = 8.1$ Hz, 2H), 8.61 (d, $J = 7.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 20.9 (CH_3), 27.3 (CH_2), 37.5 (CH_2), 62.4 (CH_2), 112.6 (C), 126.9 (CH), 128.2 (C), 131.2 (CH), 131.6 (C), 133.9 (CH), 164.1 (C=O). IR (KBr): 1730, 1693, 1663, 1589, 1447, 1389, 1347, 1241, 1057, 783 cm^{-1}. MS (70 eV): m/z 297 (M^+, 16), 222 (100), 210 (28), 198 (67), 180 (56), 153 (28), 152 (46). Found: C, 68.59; H, 5.02; N, 4.59%. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71%.

***N*-(2-Acetyloxyethyl)-1,8-naphthalimide (3):** A mixture of *N*-(2-hydroxyethyl)-1,8-naphthalimide (1.0 g, 4.1 mmol),[17] acetic anhydride (0.80 mL), and sulfuric acid (5.0 mL) was heated until it dissolved. After cooling, the solution was poured into 100 mL of 5% sodium carbonate aqueous solution and the precipitate was filtered. The crude product was purified by chromatography and recrystallized from methanol. The yield of **3** was 0.18 g (0.64 mmol, 15%). Mp 133.5–135.0 °C. ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 3H), 4.43 (t, $J = 4.9$ Hz, 2H), 4.50 (t, $J = 4.9$ Hz, 2H), 7.77 (dd, $J = 7.3$, 7.6 Hz, 2H), 8.23 (d, $J = 7.6$ Hz, 2H), 8.61 (d, $J = 7.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 20.8 (CH_3), 39.0 (CH_2), 61.9 (CH_2), 122.5 (C), 126.9 (CH), 128.2 (C), 131.3 (CH), 131.6 (C), 134.0 (CH), 164.1 (C=O), 170.8 (C=O). IR (KBr): 1745, 1696, 1656, 1589, 1437, 1375, 1232, 1048, 848, 781 cm^{-1}. MS (70 eV): m/z 283 (M^+, 26), 222 (23), 210 (37), 198 (100), 180 (47), 152 (34), 126 (24). Found: C, 67.58; H, 4.45; N, 4.78%. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94%.

***N*-(Acetyloxymethyl)-1,8-naphthalimide (4):** Naphthalimide **4** was prepared by acetylation of *N*-(hydroxymethyl)-1,8-naphthalimide (**8**): To a formalin solution (30 mL) of 1,8-naphthalimide (1.0 g, 5.1 mmol), was added a small amount of pyridine. The solution was refluxed for 2 h. After cooling, the solution was poured into 300 mL of water and the precipitate was filtered. The crude product was purified by chromatography and recrystallized from methanol. The yield of **8** was 0.96 g (4.2 mmol, 83%). Mp 252.0–254.0 °C. ^{1}H NMR ($CDCl_3$): δ 3.65 (t, $J = 8.7$ Hz, 1H), 5.76 (d, $J = 8.7$ Hz, 2H), 7.79 (t, $J = 8.5$ Hz, 2H), 8.25 (d, $J = 8.5$ Hz, 2H), 8.64 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR (DMSO-d_6): δ 62.6 (CH_2), 121.9 (C), 127.2 (CH), 127.6 (C), 130.7 (CH), 131.3 (C), 134.5 (CH), 163.2 (C=O). IR (KBr): 3407, 1698, 1661, 1589, 1509, 1459, 1340, 1240, 1059, 781 cm^{-1}. Found: C, 68.49; H, 4.07; N, 6.01%. Calcd for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.16%.

A mixture of **8** (0.50 g, 2.2 mmol), acetic anhydride (0.80 mL), and sulfuric acid (5.0 mL) was heated until it dissolved. After cooling, the solution was poured into 100 mL of 5% sodium carbonate aqueous solution and the precipitate was filtered. The crude product was purified by chromatography and recrystallized from methanol. The yield of **4** was 0.21 g (0.78 mmol, 35%). Mp 183.0–184.5 °C. ^{1}H NMR ($CDCl_3$): δ 2.10 (s, 3H), 6.25 (s, 2H), 7.79 (dd, $J = 7.3$, 8.3 Hz, 2H), 8.26 (d, $J = 8.3$ Hz, 2H), 8.66 (d, $J = 7.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 20.8 (CH_3), 63.6 (CH_2), 122.0 (C), 127.0 (CH), 128.6 (C), 131.7 (C), 131.8 (CH), 134.6 (CH), 163.5 (C=O), 169.9 (C=O). IR (KBr): 1734, 1712, 1670, 1443, 1394, 1353, 1215, 1027, 970, 780 cm^{-1}. MS (70 eV): m/z 269 (M^+, 9), 210 (34), 199 (31), 198 (100), 180 (60), 152 (35), 126 (25). Found: C, 66.54; H, 3.95; N, 5.00%. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20%.

***N*-(Methoxycarbonylmethyl)-1,8-naphthalimide (5):** Naphthalimide **5** was prepared by esterification of *N*-(carboxymethyl)-1,8-naphthalimide (**9**): A dimethylformamide (DMF) solution (250 mL) of 1,8-naphthalic anhydride (10.0 g, 51 mmol) and glycine (7.5 g) was refluxed for 6 h. After cooling, the solution was poured into 300 mL of water and the precipitate was filtered. The crude product was purified by chromatography and crystallized from acetone–ether. The yield of **9** was 5.3 g (21 mmol, 41%). Mp 272.8–273.2 °C. ^{1}H NMR ($CDCl_3$): δ 5.03 (s, 2H), 7.78 (dd, $J = 8.3$, 8.5 Hz, 2H), 8.26 (d, $J = 8.3$ Hz, 2H), 8.64 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR (DMSO-d_6): δ 41.2 (CH_2), 121.5 (C), 127.4 (CH), 127.4 (C), 131.1 (CH), 131.4 (C), 134.9 (CH), 163.1 (C=O), 169.4 (C=O). IR (KBr): 1728, 1701, 1660, 1587, 1437, 1387, 1357, 1235, 968, 777 cm^{-1}. Found: C, 65.52; H, 3.80; N, 5.17%. Calcd for $C_{14}H_9NO_4$: C, 65.88; H, 3.55; N, 5.49%.

To a methanol solution (100 mL) of **9** (3.0 g, 12 mmol), was added sulfuric acid (5.0 mL). The solution was refluxed for 1 h and poured into 300 mL of water and the precipitate was filtered. The crude product was purified by chromatography and recrystallized from methanol. The yield of **5** was 1.6 g (5.9 mmol, 51%). Mp 174.3–175.8 °C. ^{1}H NMR ($CDCl_3$): δ 3.79 (s, 3H), 4.97 (s, 2H), 7.78 (dd, $J = 7.3$, 8.5 Hz, 2H), 8.22 (d, $J = 7.3$ Hz, 2H), 8.62 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 41.2 (CH_2), 52.5 (CH_3), 122.2 (C), 126.9 (CH), 128.3 (C), 131.6 (C), 131.6 (CH), 134.3 (CH), 163.8 (C=O), 168.5 (C=O). IR (KBr): 1752, 1703, 1670, 1590, 1438, 1379, 1328, 1213, 966, 781 cm^{-1}. MS (70 eV): m/z 269 (M^+, 19), 237 (16), 210 (100), 180 (40), 154 (21), 152 (27), 126 (18). Found: C,

66.74; H, 4.13; N, 4.94%. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20%.

***N*-(Chloromethyl)-1,8-naphthalimide (6):** To a thionyl chloride solution (30 mL) of **8** (1.0 g, 4.4 mmol), was added a small amount of pyridine. The solution was refluxed for 1 h. After cooling, the solution was poured into 300 mL of water and the precipitate was filtered. The crude product was purified by chromatography and recrystallized from methanol. The yield of **6** was 1.0 g (4.1 mmol, 93%). Mp 213.0–215.5 °C. ^{1}H NMR ($CDCl_3$): δ 6.01 (s, 2H), 7.80 (t, $J = 8.3$ Hz, 2H), 8.27 (d, $J = 8.3$ Hz, 2H), 8.67 (d, $J = 8.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 47.5 (CH_2), 127.0 (C), 127.0 (CH), 131.5 (C), 131.7 (C), 131.9 (CH), 134.6 (CH), 162.7 (C=O). IR (KBr) 1710, 1679, 1586, 1436, 1308, 1235, 1137, 948, 782, 683 cm^{-1}. MS (70 eV): m/z 245 (M^+, 24), 211 (26), 210 (100), 180 (41), 154 (25), 126 (26), 63 (44). Found: C, 63.70; H, 3.55; N, 5.50%. Calcd for $C_{13}H_8ClNO_2$: C, 63.56; H, 3.28; N, 5.70%.

***N*-(Cyanomethyl)-1,8-naphthalimide (7):** A pyridine solution (150 mL) of 1,8-naphthalic anhydride (5.0 g, 25 mmol) and commercially available aminoacetonitrile monosulfate (5.3 g) was refluxed for 3 h. After cooling, pyridine was evaporated under reduced pressure. The crude product was purified by chromatography and crystallized from methanol. The yield of **7** was 4.9 g (21 mmol, 82%). Mp 254.0–256.0 °C. ^{1}H NMR ($CDCl_3$): δ 5.09 (s, 2H), 7.82 (dd, $J = 8.3$, 8.5 Hz, 2H), 8.29 (d, $J = 8.5$ Hz, 2H), 8.67 (d, $J = 8.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 27.3 (CH_2), 114.6 (CN), 121.6 (C), 127.8 (CH), 128.2 (C), 131.7 (C), 132.1 (CH), 135.7 (CH), 162.9 (C=O). IR (KBr): 2252, 1703, 1667, 1585, 1437, 1377, 1323, 1239, 1181, 778 cm^{-1}. MS (70 eV): m/z 236 (M^+, 67), 182 (74), 154 (100), 127 (27), 126 (64), 63 (36), 50 (15). Found: C, 70.92; H, 3.44; N, 11.70%. Calcd for $C_{14}H_8N_2O_2$: C, 71.18; H, 3.41; N, 11.86%.

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