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Dyes and Pigments 57 (2003) 21–28
DYES and PIGMENTS
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Luminescent properties and photo-induced electron transfer of naphthalimides with piperazine substituent

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Received 18 September 2002; received in revised form 12 October 2002; accepted 21 November 2002

Abstract

Novel piperazine substituted naphthalimide model compounds 2-methyl-6-(4-methyl-piperazin-1-yl)-benzo[*de*] isoquinoline-1,3-dione (**NA1**), 2-methyl-6-(4,4-dimethyl-piperazin-1-yl)-benzo[*de*] isoquinoline-1,3-dione iodide **(NA2)** and 2-methyl-6-(4-methyl-piperazin-1-yl)-benzo[*de*] isoquinoline-1,3-dione hydrochloride (**NA3**) were synthesized. Fluorescence spectra data of **NA1** showed the fluorescence quantum yields plot of **NA1** versus pH value is typically characteristic of pH probe. The approximate free energy of charge separation (ΔG_{cs}) for the excited singlet state and the fluorescent lifetime data of **NA1** showed that the fluorescence of 4-amino-1,8-naphthalimide fluorophore can be quenched by the PET process from the alkylated amine donor to the naphthalimide moiety. The PET path can be obviously switched off either by the protonation (as for **NA3**) or quarternization (as for **NA2**) of the alkylated amine donor.

Keywords: Fluorescent probe; Photo-induced electron transfer; Synthesis; 1,8-Naphthalimide; Fluorescent lifetime

1. Introduction

Protons were used extensively as external stimulus in the design and construction of molecular signaling systems [1–4]. Protonation of an aromatic amine or an alkylated amine group in fluorophore-amine conjugates may result in the elimination of charge transfer or photo-induced electron transfer (PET) [5,6]. Recently, we used the 4-amino-1,8-naphthalimide fluorophore to design dual-mode protons/electrochromic molecular switches and functional fluorescent imaging polymers [7–9]. In these derivatives, the node at the N-imide atom [10], which blocks PET from amine electron donor to the N-imide is avoid. Protonation of the alkylated amines in these compounds will "switch off" the PET path and recover the fluorescence of the 4-amino-1,8-naphthalimide fluorophore.

In this report, model compounds **NA1**, **NA2** and **NA3** were prepared to confirm the PET process in these derivatives. In the model compound**NA1**, the PET process occurs from the alkylated amine donor to the 4-amino-1,8-naphthalimide fluorophore through the piperazinyl ring. The fluorescence of the 4-amino-1,8-naphthalimide

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0143-7208/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0143-7208(02)00162-6

fluorophore is quenched. The PET path can be switched off either by the protonation or quaterization of the amine, and the fluorescence of the naphthalimide fluorophore is then recovered (Fig. 1). Their spectral properties as a function of pH values were investigated. The approximate free energy of charge separation (the driving force, ΔGcs) for the excited singlet states of NA1 showed that the photo-induced electron transfer from the alkylated amine donor to 4-amino-1,8-naphthalimide fluorophore is thermodynamically feasible. The fluorescence lifetime data of NA1 and NA2 were measured by single-photon counting technique.

2. Experimental

2.1. General

Melting points were measured on a X4 Micro-melting point apparatus. NMR spectra were obtained using a Bruker AM 500 spectrometer. ^{13}C NMR spectra were obtained operating at 125.75 MHz. Mass spectra were obtained with HP5989A, Mariner API time of flight (TOF, TIS ion source, PE Corp.) and API2000 (TIS, PE Corp.) spectrometers. Infrared spectra were measured on a Nicolet Magna IR550. UV–vis–NIR spectra were recorded on a Varian Cary500. Fluorescence spectroscopy was recorded on a Varian Cary Eclipse Fluorescence Spectrophotometer. Fluorescence lifetimes of compounds were measured by single-photon counting technique (Edinburgh FL 900) with a hydrogen-filled flash lamp and deconvolution method. The temporal resolution after deconvolution of the exciting pulse is ~200 ps. The starting compound 6-bromo-2-methyl-benzo[*de*] isoquinoline-1,3-dione (BMBI) was prepared by the reaction of 4-bromo-1,8-naphthalic anhydride with 10% aqueous methylamine at room temperature for 2.5 h, pure product could be recrystallized from benzene chloride.

2.2. Preparation of 2-methyl-6-(piperazin-1-yl)-benzo[de] isoquinoline-1,3-dione (*NA0*)

Five grams BMBI (17 mmol) and 5.1 g piperazine hydrate (26 mmol) in 20 ml methoxyl ethanol was refluxed for 3 h. The mixture was allowed to stand overnight at room temperature. The yellow solid obtained was filtered off. The crude product was dissolved in hot mixture solvent of minim water and ethanol, and undissolved residual was filtered off. Four grams pure crystals were obtained by adding ether to the above solution with a yield of 78.4%. Mp 200–202 °C. ^1H NMR (in DMSO-d_6) δ (ppm): 8.42 (t, $J=7.01$, $J=8.16$ Hz, 2H), 8.35 (d, $J=8.09$ Hz, 1H), 7.76 (t, $J=7.62$, $J=8.08$ Hz, 1H), 7.27 (d, $J=8.10$ Hz, 1H), 3.36 (s, 3H, $-CH_3$), 3.14 (t, 4H, $-N(CH_2)_2-$), 2.99 (t, 4H, $HN(CH_2)_2-$). Anal. calc. for $C_{17}H_{17}N_3O_2$: C, 69.17; H, 5.76; N, 14.23%. Found: C, 68.75; H, 5.76; N, 14.17%.

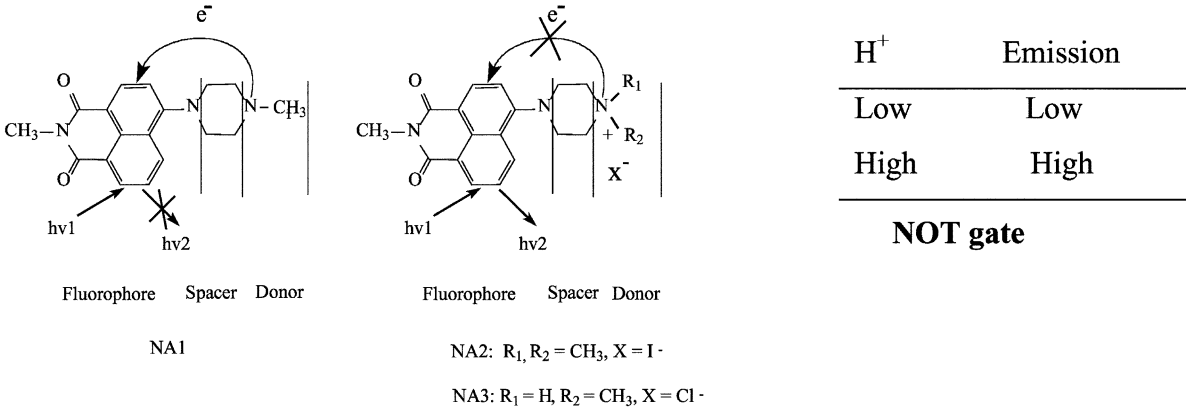


Fig. 1. Photo-induced electron transfer path in **NA1**, **NA2** and **NA3** and the logic gate made by them.

2.3. Preparation of 2-methyl-6-(4-methyl-piperazin-1-yl)-benzo[de] isoquinoline-1,3-dione (*NA1*)

Paraaldehyde (0.3 g) (amount to 10 mmol formaldehyde) was added to a solution of 1.5 g **NA0** (5 mmol) in 10 ml formic acid (88%), with stirring at 80 °C for 20 h. Then all solvent was removed by vacuum. To the residual, 20 ml 3 N hydrochloric acid was added, and the solution was refluxed for 1 h. Sodium carbonate powder was added carefully, yellow solid was obtained. Pure crystals (1.2 g) were obtained by recrystallization from ethanol with a yield of 77.8%. Mp 179–180 °C. ^{1}H NMR (in DMSO-d_6) δ (ppm): 8.47 (d, $J=7.25$ Hz, 1H), 8.42 (d, $J=8.46$ Hz, 1H), 8.38 (d, $J=8.09$ Hz, 1H), 7.80 (dd, $J=7.30$, $J=7.30$ Hz, 1H), 7.33 (d, $J=8.11$ Hz, 1H), 3.38 (s, 3H, –CH_3), 3.26 (t, 4H, –N(CH_2)$_2$), 2.65 (t, 4H, HN(CH_2)$_2$–), 2.09 (s, 3H, –(CH_2)$_2$N–CH_3). ^{13}C NMR (in DMSO-d_6) δ (ppm): 163.73, 163.20, 155.30, 131.96, 130.45, 128.88, 125.96, 125.23, 122.48, 115.62, 115.07, 54.38, 52.11, 45.29, 26.51. MS (EI, 70 eV) m/z (%) $[M+1]^+$ 310 (32.8), $[M]^+$ 309 (100), 238 (11.7), 224 (12.5).

2.4. Preparation of 2-methyl-6-(4,4-dimethyl-piperazin-1-yl)-benzo[de] isoquinoline-1,3-dione iodide (*NA2*)

Methyl iodide (5 ml) was added to a solution of 1 g **NA0** (3.4 mmol) in 30 ml methanol with stirring at room temperature for 30 min, then refluxed for 1 h, yellow solid was obtained by adding 10 ml aqueous sodium carbonate (20%), 1.4 g pure compound was obtained by recrystallization from water with a yield of 91.6%. Mp 296–298 °C. ^{1}H NMR (in DMSO-d_6) δ (ppm): 8.51(t, $J=7.21$, $J=7.01$ Hz, 2H), 8.46 (d, $J=8.02$ Hz, 1H), 7.36 (t, $J=7.38$, $J=7.39$ Hz, 1H), 7.51 (d, $J=8.06$ Hz, 1H), 3.77 (t, 4H, –N(CH_2)$_2$–), 3.62 (t, 4H, HN(CH_2)$_2$–), 3.39 (s, 3H, –CH_3), 3.32 (s, 6H, –N^+(CH_3)$_2$–). ^{13} C NMR (in DMSO-d_6) δ (ppm): 163.65, 163.16, 153.55, 131.69, 130.62, 130.23, 128.72, 126.45, 125.33, 122.56, 116.90, 116.32, 60.79, 51.07, 46.04, 26.57. Anal. calc. for $C_{19}H_{22}IN_3O_2$: C, 50.59; H, 4.88; N, 9.31% Found: C, 50.48; H, 4.87; N, 9.22%.

2.5. Preparation of 2-methyl-6-(piperazin-1-yl)-benzo[de]isoquinoline-1,3-dione hydrochloride (*NA3*)

NA0 (1 g, 3.4 mmol) was dissolved in 20 ml 95% aqueous ethanol, then 20 ml 3 N hydrochloric acid was added. All solvent was distilled by vacuum to get **NA3**. 1 g pure product was obtained by recrystallization from 95% aqueous ethanol with a yield of 88.9%. mp 284 °C (decomp.). ^{1}H NMR (in DMSO-d_6) δ (ppm): 7.69 (d, $J=8.42$ Hz, 1H), 7.39 (d, $J=7.08$ Hz, 1H), 7.32 (d, $J=7.93$, Hz, 1H), 7.10 (t, $J=7.89$, $J=7.55$ Hz, 1H), 6.70 (d, $J=8.01$ Hz, 1H), 3.43 (t, 4H, –N(CH_2)$_2$–), 3.2 (t, 4H, HN(CH_2)$_2$–). 2.71 (s, 3H, –CH_3). Anal. calc. for $C_{17}H_{18}ClN_3O_2$: C, 61.57; H, 5.43; N, 12.67%. Found: C, 61.47; H, 5.39; N, 12.59%.

3. Results and discussion

Naphthalimide derivatives have high fluorescent quantum yield [10]. Recently, they were used as supramolecular moieties to design proton sensors for the study of photo-induced electron transfer [11–15]. Generally, these model compounds are constructed in the form donor–spacer–fluorophore (D–S–F), in which a tertiary amine is always selected as the donor. The donor can be linked through spacer on the *N*-imide or on the 4-position of the naphthalene ring. With the same tertiary amine donor and the same 4-amino-1,8-naphthalimide fluorophore, the driving force (ΔG_{cs}) for the PET process in the two kinds of PET model compounds are almost the same. Estimated from the measured redox potentials of the couples using the Weller equation [$\Delta G_{cs}=E_{ox}(D)-E_{Red}(F)-E_{0,0}$], the driving force for the PET process is calculated to be −6.6 kcal/mol [15,16], in which the triethylamine is selected as the donor. This indicates that ΔG_{cs} for NA1 is sufficiently negative for PET from the alkylated tertiary amine donor to the 4-amino-1,8-naphthalimide fluorophore. Since the unidirectional repulsive electric field existing in the naphthalimide is avoided, it can be expected that the fluorescence of the naphthalimide fluorophore in **NA1** would be obviously quenched by PET from the alkylated amine donor to the naphthalimide moieties.

As aminoalkyl substituted fluorescent proton sensor, **NA1** showed weak fluorescence in basic solution (Fig. 2), protonation of the alkylated amine in **NA1** stops the PET process and the fluorescence of the 4-amino-1,8-naphthalimide fluorophore increases gradually with the decrease of the pH value. Since its plot of fluorescence quantum yields versus pH value shown in Fig. 2 is typically characteristic of pH probe, this kind of piperazine substituted naphthalimides can be used in the design of molecular signaling systems.

The absorption and fluorescence emission spectra data of **NA1** and **NA2** were listed in Table 1. As seen in Figs. 3 and 4. Protonation of the alkylated amine donor in NA1 drastically alters the electron-donating properties and consequently switching of the PET path from the alkylated amine donor to the 4-amino-1,8-naphthalimide moiety. The typical naphthalimide absorption bands and emission bands of **NA1** in methanol/water (1:4 v/v) are blue-shifted upon-protonation and red-shifted upon deprotonation (Fig. 3). However, the naphthalimide absorption and emission bands of **NA2** are almost unchanged upon protonation and deprotonation (Fig. 4). Compared with the fluorescence at pH 11, protonation of the alkylated amine of **NA1** results in the fluorescence enhancement of the 4-amino-1,8-naphthalimide fluorophore by 76.3 times.

Table 1
Absorption and fluorescence spectra data of **NA1** and **NA2**

Compound	NA1	NA2
λ_{ab}^{max}/nm (pH = 2.3)	388.4	386.8
λ_{ab}^{max}/nm (pH = 7.0)	398.5	387.5
λ_{ab}^{max}/nm (pH = 11.0)	408.0	387.8
λ_{Em}^{max}/nm (pH = 2.3 excited at 388.4 nm)	524.4	524.7
λ_{Em}^{max}/nm (pH = 7.0 excited at 388.4 nm)	533.4	524.2
λ_{Em}^{max}/nm (pH = 11.0 excited at 388.4 nm)	541.6	524.7
φ_f (pH = 2.3)	0.66	0.58
φ_f (pH = 7.0)	0.29	0.57
φ_f (pH = 11.0)	0.0086	0.57
FE* = φ_{flu} (pH = 2.3)/φ_{flu} (pH = 11.0)	76.3	1.0

*Factor for proton-induced fluorescence enhancement. The fluorescence quantum yield φ_f vs. pH for **NA1** and **NA2** are performed on excitation at 388.4 nm with the concentration of 10^{-5} M in aerated methanol: water (1:4, v/v). Rhodamine B is employed as an internal standard and its fluorescence quantum yield is defined as $\varphi_{f\,(RhB)} = 1$. The fluorescence quantum yields are calculated using the relationship: $\varphi_f = \varphi_{f\,(RhB)}(A_{(RhB)}/A)\,(I/I_{RhB})$ where $A_{(RhB)}/A$ represents the ratio of the absorbance of Rhodamine B to that of sample in aerated methanol/water (1: 4, v/v) at 388.4 nm, and I/I_{RhB} represents the ratio of the integral fluorescence peak area (450–670 nm) of sample to that of Rhodamine B excited at 388.4 nm in aerated methanol: water (1:4, v/v).

The PET path in model compound **NA1** can also be switched off by quarternization of the alkylated amine. **NA2** was synthesized by direct quaternization of the secondary amine in **NA0** with methyl iodide. The PET process is locked in

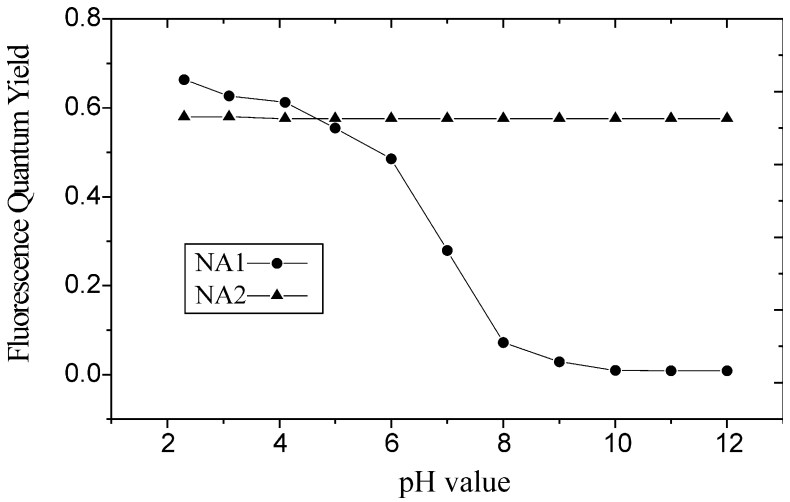


Fig. 2. Relative fluorescence quantum yields φ_{flu} versus pH for **NA1**, **NA2**. Excited at 388.4 nm in aerated MeOH:H_2O (v/v = 1:4).

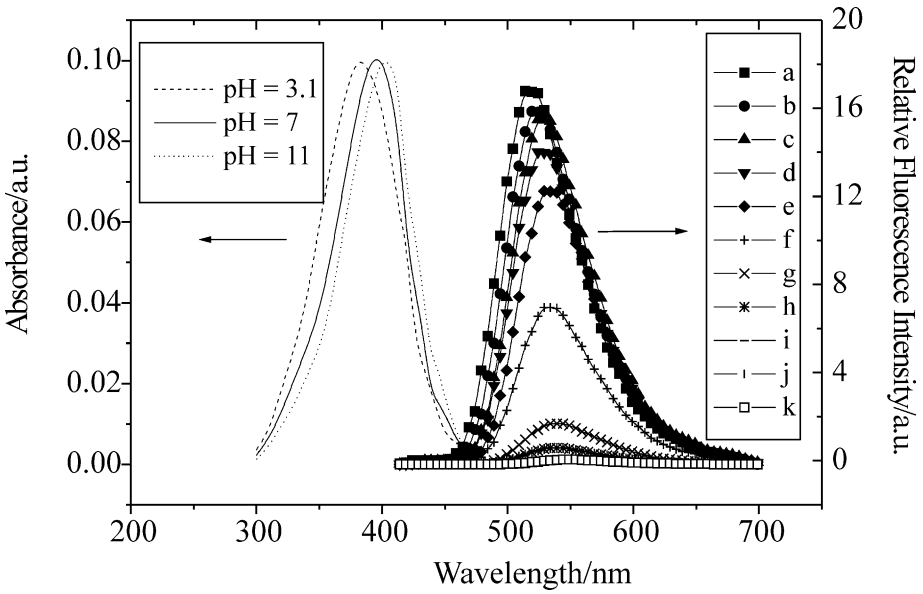


Fig. 3. Absorption and fluorescent emission spectra of **NA1** in methanol/water (1:4 v/v) at different pH value: (a) 2.3 (b) 3.1 (c) 4.1 (d) 5 (e) 6 (f) 7 (g) 8 (h) 9 (i) 10 (j) 11 (k) 12.

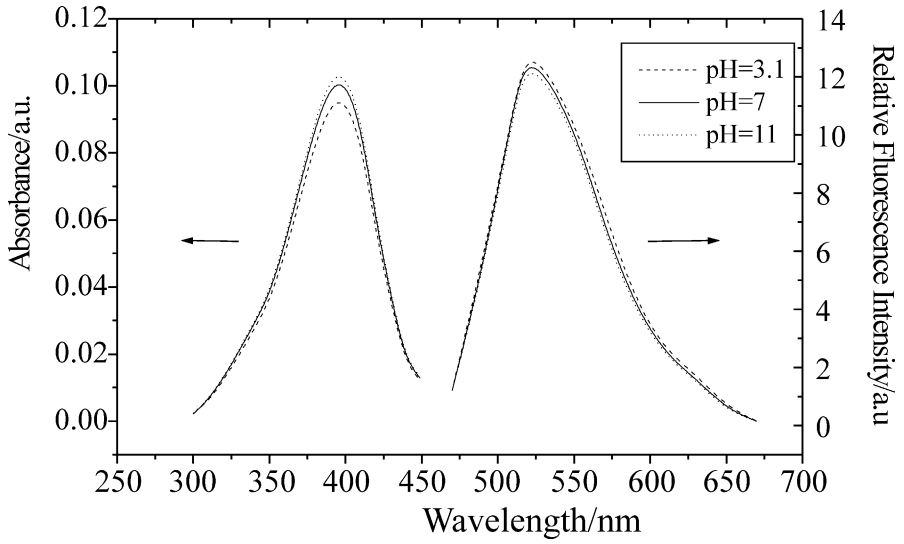


Fig. 4. Absorption and fluorescent spectra of **NA2** in methanol/water (1:4 v/v) at different pH value.

the status of "off", and the fluorescence of the 4-amino-1,8-naphthalimide is recovered. Fig. 4 showed that the fluorescence of **NA2** is almost intrinsically characteristic for pH-independence.

The excited states of some fluorescent compounds undergo conformational adjustment following charge transfer, and this movement in generally deactivates the singlet state of the fluorophore. The conformation of the piperazinyl ring in the model compounds **NA1** and **NA2** interconverts between the chair type and the boat type. If the fluorescence of these compounds is influenced by the conformation adjustment between the chair type and the boat type of the piperazinyl

ring, the fluorescence of these compounds will vary with the viscosity. According to Fig. 5, the fluorescence of **NA3** is almost intrinsically characteristic for viscosity-independence. It can expected that the conformational adjustment in these model compounds does not influence the fluorescence of the fluorophore and rotation about the C–N bond joining the piperazine ring and the naphthalimide moiety is restricted by the peric hydrogen atom of the naphthalimide ring [17]. This can give further evidence that the fluorescence quenching of the 4-amino-1,8-naphthalimide fluorophore of **NA1** is caused indeed by the PET process from the alkylated amine donor to the naphthalimide fluorophore.

The fluorescence lifetime data of the **NA1** and **NA2** in acetonitrile were listed in Table 2. As seen in Fig. 6, their fluorescence emission decays according to bi-exponential kinetics. The short component represents the lifetime of the PET quenched state and the long-lived component represents the back electron transfer to the ground state. The short components of **NA2** in acetonitrile and in methanol are 1.02 and 1.5 ns longer than the short components of **NA1**, respectively. This may be ascribed to the "switching off" of the PET process from the alkylated amine donor to the 4-amino-1,8-naphthalimide fluorophore. The low percentages of short components observed in the case of**NA2** confirm the inefficient PET communication in **NA2**.

Table 2
Fluorescence lifetime data of the **NA1** and **NA2** (excited at 360 nm)

Compound	Solvent	E_m (nm)	τ_1 (%) ns	τ_2 (%) ns
NA1	Acetonitile	520	5.37 (36.0)	0.38 (64.0)
	Methanol	540	9.0 (80.6)	0.21 (19.4)
	Ethyl acetate	520	6.7 (84.3)	0.50 (15.7)
	Cyclohexane	470	6.9 (100)	
NA2	Acetonitrile	510	8.77 (97.5)	1.43 (2.5)
	Methanol	510	8.7 (95.6)	1.8 (4.4)

The PET process in is largely influenced by the polarity of solvents, because PET is considerably accelerated in polar media for 4-amino-1,8-naphthalimides and the short components of **NA1** are diminished in a solvent with low polarity. As in cyclohexane, the short component of **NA1** is not observed.

In conclusion, the fluorescence of **NA1** is quenched by the PET process from the alkylated amine donor to the 4-amino-1,8-naphthalimide fluorophore. The PET path in **NA1** can be switched off either by the protonation (as for **NA3**) or quarternization (as for **NA2**) of the alkylated amine donor. Luminescent properties of **NA1** showed that this kind of piperazine substituted naphthalimide compounds may be used in the design of molecular signaling systems, because the fluorescence of the

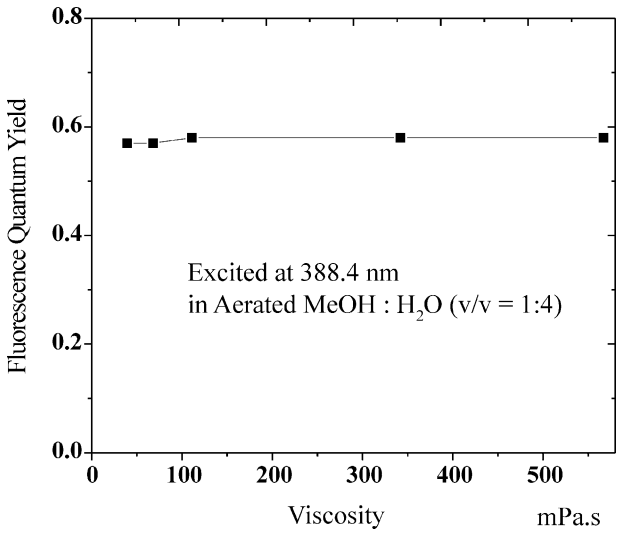
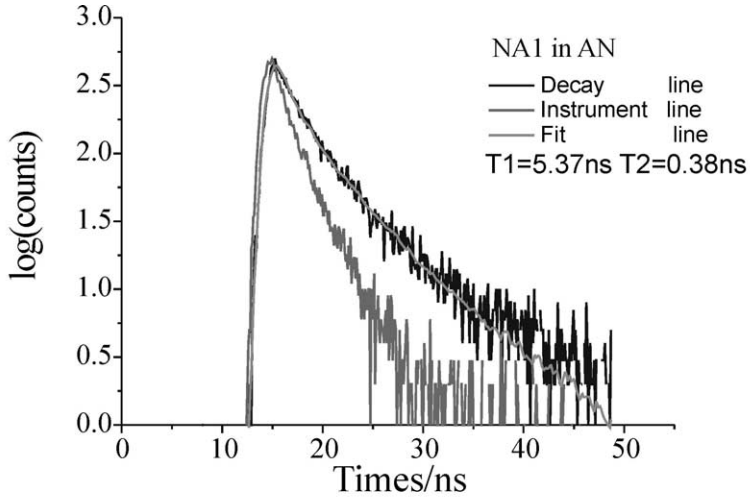


Fig. 5. Relative fluorescence quantum yields φ_f versus viscosity for **NA3**.



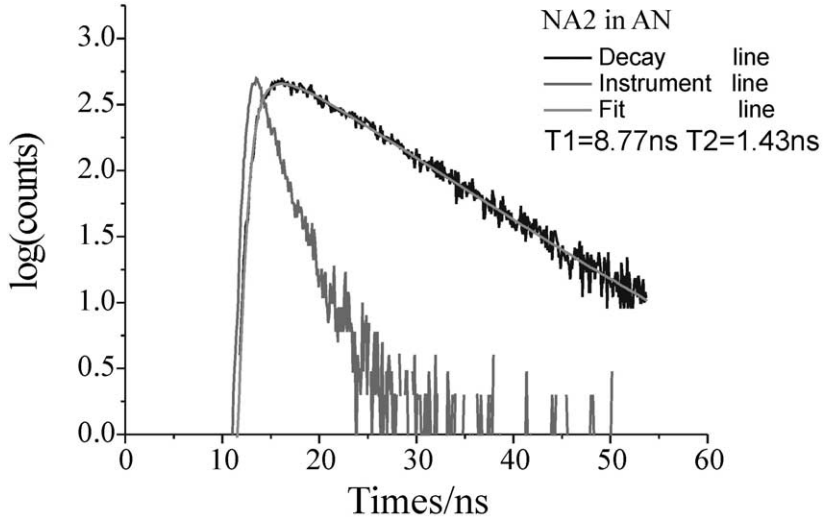


Fig. 6. Fluorescence decay profile of **NA1** and **NA2** in acetonitrile (AN) excited at 360 nm. (For **NA1**, emission wavelength is 520 nm and for **NA2**, emission wavelength is 510 nm.)

naphthalimide fluorophore can be recovered by the stimulation of the protons by 76.3 times.

Acknowledgements

This research was supported by NSFC/China and Education Ministry of China and Education Committee of Shanghai.

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