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A proton sponge-based fluorescent switch

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Abstract—A proton-triggered fluorescent switch was developed through direct connection of a proton sponge, 1,8-bis(dimethylamino)naphthalene to a fluorophore, 4-aminonaphthalimide. The molecular fluorescent switch was based on a photoinduced electron transfer (PET) mechanism. The fluorescent switch exhibited significant fluorescence enhancement upon binding the low-concentration protons in high pH aqueous solution. The high pK_a value (around 11) of the fluorescent switch could be ascribed to the nature of the proton sponge.

The fluorescent signaling recognition of proton has become an active area of investigation, in a view of its basic interest and many potential applications. Quite a few fluorescent switches triggered by proton have been successfully developed as sensing and imaging reagents[1] and recently, this technique has even been applied in the single molecule spectroscopy studies.[2] And also, they have been used as the key components of various molecular logic devices for information processing.[3]

So far, for most proton-triggered fluorescent switches, the receptor units that bind protons are the ordinary aliphatic or aromatic amines, or some nitrogen-containing heterocycles like pyridine. These weakly basic receptors have relatively low pK_a values (3–8),[4] which are suitable for biological applications. However, for other applications, these switches might not be sensitive enough, particularly in the material science field. Because, if the proton concentration is lower ($<10^{-8}$ mol/L, e.g., in solid films, organic solvents or in higher pH aqueous solutions), the recognition process (protonation) will not occur and therefore, these switches cannot work. For example, the important novel application of proton-triggered fluorescent switches to map photoacid in films might possibly suffer from such a limitation: the fluorescent switches and certain photoacid-generators have been dispersed in polymer films. After light irradiation, patterned fluorescent images would be formed, because proton released in situ from the decomposed photoacid-generators was immediately trapped by the proton receptor units of the fluorescent switch molecules and affected the spectroscopic properties of the latter. However, due to the low pK_a of the proton-triggered fluorescent switches, a rather large amount of photoacid-generator was required to meet the concentration proton necessary for the protonation process.[5] Obviously, the high ratio of photoacid-generators is not economical and might possibly affect the properties of the films. The use of stronger organic bases as the receptor units was expected to improve the sensitivity of the proton-triggered fluorescent switches. But so far, no such attempt has been reported.

1,8-Bis(dimethylamino)naphthalene, **DMAN**[6] the first and most important member of the proton sponge family, could be the proper candidate as the efficient proton receptor, considering its exceptionally high basicity ($pK_a = 12.1$ in water). **DMAN** is theoretically interesting: based on previous investigation many derivatives and analogs have been prepared for enhanced basicity.[7] Also, **DMAN** is synthetically useful as efficient non-nucleophilic basic catalyst.[8] But, the applications of **DMAN** and other proton sponge were rather limited in organic synthesis. In this investigation, our attempt to use **DMAN** as the receptor of a fluorescent switch

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Keywords: Fluorescent switch; Proton sponge; Photoinduced electron transfer.

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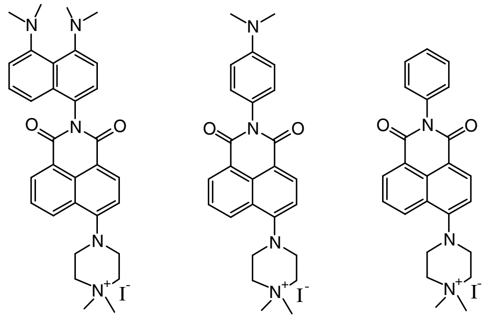


Scheme 1. The structures of the studied compounds.

might possibly be the beginning for novel applications of the proton sponges in supramolecular chemistry.

The molecular design of the new proton-triggered fluorescent switch, compound **1** (shown in Scheme 1), was based on the photoinduced electron transfer (PET) motif.[9] The **DMAN** moiety was directly connected to the 9-imide nitrogen of the 4-aminonaphthalimide for the purpose to form the virtually electronically-decoupled receptor–fluorophore system.[10] The electron-rich **DMAN** unit would play dual roles as the electron donor and the proton receptor. The PET process from the proton-free **DMAN** unit to the 4-aminonaphthalimide would quench the fluorescence of the latter; upon the **DMAN** unit bonding a proton, fluorescence intensity would be enhanced drastically due to the inhibition of the PET process. For the accurate determination of pH effect to the fluorescence intensity, a quaternary ammonium was incorporated on the 4-amino position to improve the water solubility. Reference compounds **2** with a dimethylanilino group as electron donor and proton receptor, and **3** without electron donor were designed for comparisons. From the starting material **DMAN**, targeted compound **1**[11] was efficiently synthesized via a 5-step procedure, as illustrated in Scheme 2. The reference compounds **2** and **3** were also synthesized via similar procedures.

The spectral properties of compounds **1**–**3** in water under different pH were studied. The three compounds exhibited similar absorption spectra (not shown here), which did not shift upon the pH change. The band in VIS range had one maximum around 420 nm, which could be ascribed to the absorption of the 4-disubstituted-aminonaphthalimide chromophore.[12] In a strongly basic solution, the receptors could not bind proton, but the absorption spectra of **1** and **2** are similar to that of **3**, indicating that there was no (or very weak) ground-state electronic interaction between the donor units (**DMAN** for **1**, and dimethylanilino group for **2**) and the acceptor naphthalimide fluorophore, as was expected for the virtually decoupled systems.

The fluorescence spectra of **1**–**3** under different pH were also measured. The fluorescence spectra of **1** were recorded in Figure 1. Although the band maximum around 530 nm did not shift remarkably and was similar to that of compound **3**, the fluorescence intensity was strongly dependent on the pH value. The fluorescence was very low when pH >13, indicating that the PET interaction between the proton-free **DMAN** unit and the naphthalimide acceptor occurred efficiently. In the basic range (pH = 10–13), as the pH value decreased,

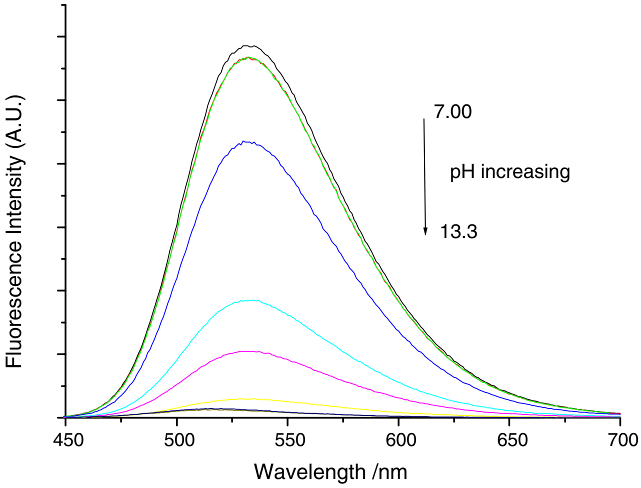
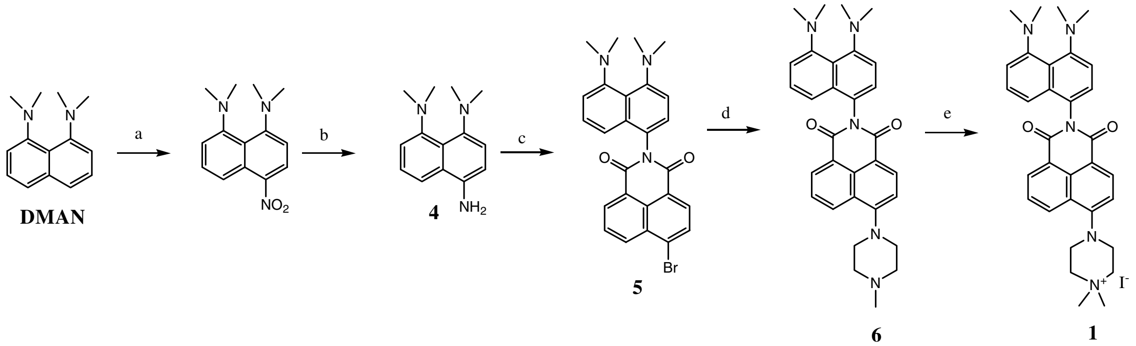


Figure 1. Normalized fluorescence spectra of 1 (5×10^{-6} M) in water solution of different pH values, from top to bottom pH = 7.00, 8.50, 9.88, 10.5, 11.1, 11.5, 12. 3, 12.9, 13.3.



Scheme 2. Synthesis of **1**. Reagents and conditions: (a) $NaNO_3$, H_2SO_4, −5 °C, yield 58%; (b) H_2, Pd–C, ethanol, rt, yield 85%; (c) 4-bromonaphthalic anhydride, propyl acid, reflux, yield 56%; (d) *N*-methylpiperazine, 2-methoxyethanol, reflux, yield 88%; (e) CH_3I, dichloromethane, rt, yield 42%.

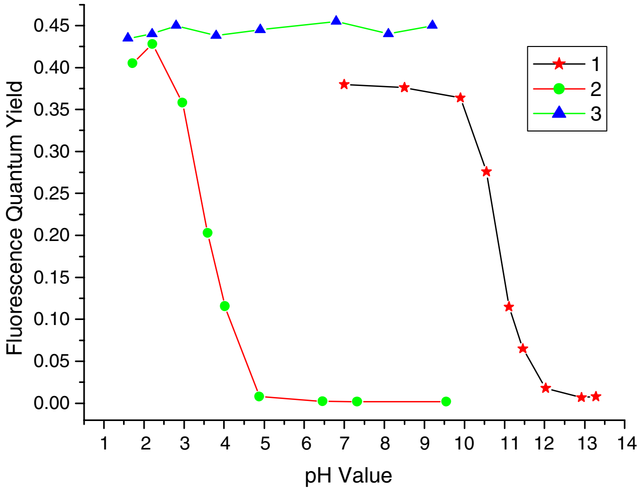


Figure 2. The fluorescence quantum yield versus pH for compounds **1**–**3**.

the fluorescence intensity increased dramatically, indicating that the protonation of the **DMAN** could block the PET process and so fluorescence recovered; in the range of pH <10, the fluorescence intensity was constantly strong. The fluorescence quantum yields were also determined and plotted in Figure 2. The fluorescence at pH = 10 ($\Phi = 0.38$), is about 52-folds higher than that at pH = 13 ($\Phi = 0.007$). Such significant difference in fluorescence intensity indicated that **1** was an efficient fluorescent switch triggered by proton in aqueous solution. Compound **2** also exhibited the similar fluorescence 'off–on' properties in aqueous solution, but, as shown in Figure 2, the proton-signaling range has shift to acidic range (pH = 2–5). Compound **3** had stable and strong fluorescence ($\Phi = \sim 0.45$) independent on the pH, because it, unlike **1** and **2**, had no proton receptor and electron donor necessary for the PET processes.

The pK_a values of **1** and **2** were determined from the pH–Φ curves at around 11 and 3, respectively. The high pK_a value of **1** suggested that it could respond to the extremely low-concentration proton, is unprecedented for PET fluorescent switches and should be ascribed to the **DMAN** receptor without doubt. With the high pK_a value, **1** and analogs might find important applications in material science. For example, they could be more sensitive proton-driven logic devices than existing ones. Therefore, less photoacid-generators might be required compared with other reported fluorescent proton-trappers, if they are used in the fluorescent imaging in polymeric films.

In summary, we have proved that the proton sponge **DMAN** could be used as the receptor unit to develop sensitive fluorescent switches triggered by lower-concentration proton. The new PET fluorescent switch **1** based on **DMAN**, exhibited significant fluorescence enhancement upon protonation in high pH aqueous solutions. The idea on designing a fluorescent switch could be borrowed for the development of other kinds of functional materials whose properties might be sensitively modulated by protonation. Now the development of highly sensitive photoacid trapper for the fluorescent imaging in polymer films is in progress in our laboratory.

Acknowledgement

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11. Compound **1**: mp 298–300 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 2.80$ (s, 6H), 2.84 (s, 6H), 3.37 (s, 6H), 3.65 (br s, 4H), 3.81 (br s, 4H), 6.95–6.97 (d, $J = 7.2$ Hz, 1H), 7.03–7.06 (m, 2H), 7.18–7.22 (t, $J = 7.8$ Hz, 1H), 7.33–7.35 (d, $J = 8.0$ Hz, 1H), 7.55–7.57 (d, $J = 8.4$ Hz, 1H), 7.90–7.94 (t, $J = 7.8$ Hz, 1H), 8.47–8.49 (d, $J = 8.0$ Hz, 1H), 8.52–8.54 (d, $J = 7.2$ Hz, 1H), 8.59–8.61 (d, $J = 8.4$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 43.96$, 44.02, 46.12, 60.84, 111.72, 112.66, 114.95, 116.43, 117.41, 119.68, 123.17, 125.55, 125.64, 126.44, 126.62, 129.65, 130.57, 131.03, 132.07, 133.34, 150.60, 150.73, 153.88, 163.59, 164.08 ppm; IR (KBr) 1700, 1660, 1575, 1369 cm^{-1}; ESI-MS *m*/*z* 523 (M^{+}), 262 ($M^{+}+H^{+}$); HR-MS *m*/*z* calcd for $C_{32}H_{36}N_5O_2^{+}{*}H^{+}$: 261.6473. Found:

261.6477. Compound **2**: mp 308–310 °C; ^{1}H NMR (400 MHz, DMSO-d_6) $\delta = 2.97$ (s, 6H), 3.31 (s, 6H), 3.62 (br s, 4H), 3.79 (br s, 4H), 6.80–6.82 (d, $J = 8.8$Hz, 2H), 7.10–7.12 (d, $J = 8.8$ Hz, 2H), 7.52–7.54 (d, $J = 8.0$ Hz, 1H), 7.87–7.91 (t, $J = 7.6$ Hz, 1H), 8.46–8.48 (d, $J = 8.0$ Hz, 1H), 8.50–8.52 (d, $J = 7.2$ Hz, 1H), 8.54–8.56 (d, $J = 8.8$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 46.09$, 60.85, 112.20, 116.63, 117.62, 123.34, 124.33, 125.25, 126.54, 129.21, 130.27, 130.85, 131.87, 150.00, 153.29, 163.55, 164.04 ppm; IR (KBr): 1701, 1655, 1589, 1371, 1240 cm^{-1}; ESI-MS: m/z calcd 429, [M$^+$]; HR-MS: m/z calcd for $C_{26}H_{29}N_4O_2^+$: 429.2291. Found: 429.2292. Compound **3**. The synthesis was similar to that of compound **1**: mp 280–282 °C; ^{1}H NMR (400 MHz, DMSO-d_6) $\delta = 3.34$ (s, 6H), 3.64 (br s, 4H), 3.82 (br s, 4H), 7.35–7.37 (d, $J = 7.6$ Hz, 1H), 7.46–7.48 (d, $J = 7.2$ Hz, 1H), 7.51–7.57 (m, 3H), 7.87–7.91 (t, $J = 8.0$ Hz, 1H), 8.46–8.48 (d, $J = 8.4$ Hz, 1H), 8.51–8.53 (d, $J = 7.2$ Hz, 1H), 8.57–8.59 (d, $J = 8.4$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 45.94$, 60.76, 116.22, 117.26, 122.96, 125.41, 126.28, 127.84, 128.53, 128.85, 129.23, 130.22, 130.59, 131.61, 135.80, 153.53, 162.94, 163.45 ppm; IR (KBr): 1702, 1657, 1590, 1370, 1240 cm^{-1}; ESI-MS: m/z calcd 386, [M$^+$]; HR-MS: m/z calcd for $C_{24}H_{24}N_3O_2^+$: 386.1869. Found: 386.1870.

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