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# UNEXPECTED FLUORESCENT BEHAVIOR OF A NEW PH CHEMOSENSOR BASED UPON BIS-4-PIPERIDINE-1,8-NAPHTHALIMIDE LINKED BY THE DIETHYLENETRIAMINE

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**Dedicated to Professor Dr. Albert Eschenmoser on the occasion of his 85th birthday**

**Abstract** – A new fluorescent chemosensor **3** based upon bis-4-piperidine-1,8-naphthalimide linked by the diethylenetriamine was synthesized, and its fluorescent properties were also investigated. Different from other bis-1,8-naphthalimides, no changes in the fluorescence spectra of **3** in the presence of metal cations was observed, and it displayed an unexpectedly strong fluorescence quench in weakly acidic aqueous solutions. Its p*Ka* value (7.25) indicated that it would be suited as a new pH fluorescent chemosensor to monitor changes at the physiological pH range.

## INTRODUCTION

Currently, the design and synthesis of fluorescent devices for the sensing and reporting chemical species is of very importance for biological and environmental applications.[1-5] Due to their fluorescent properties and special interactions with some biomolecules, mono-1,8-naphthalimides are frequently used as the fluoroionophores to prepare fluorescent chemosensors for metal cations and protons.[6-9] To the best of our knowledge, however, little attention has been paid to the fluorescent properties of the bis-1,8-naphthalimides. Chovelon *et al.* described the changes in the fluorescence spectra of bis-1,8-naphthalimide analog **1** (Figure 1) in the presence of metal cations ($Zn^{2+}$, $Ni^{2+}$ and $Ce^{3+}$) and protons.[10] Staneva *et al.* reported $Fe^{3+}$ and $Cr^{3+}$-induced fluorescence spectra changes of bis-1,8-naphthalimide analog **2** (Figure 1).[11] Obviously, introducing the different groups (*e.g.*, *N*,*N*-dimethylaminoethylamino group) on the 4-position of **1** could lead to compound **2** with different photophysical properties. Therefore, in this paper we want to introduce the piperidine group on the 4-position of **1**, and investigate the fluorescent properties of a new bis-1,8-naphthalimide analog **3** (Figure 1) based on bis-4-piperidine-1,8-naphthalimide linked by the diethylenetriamine.

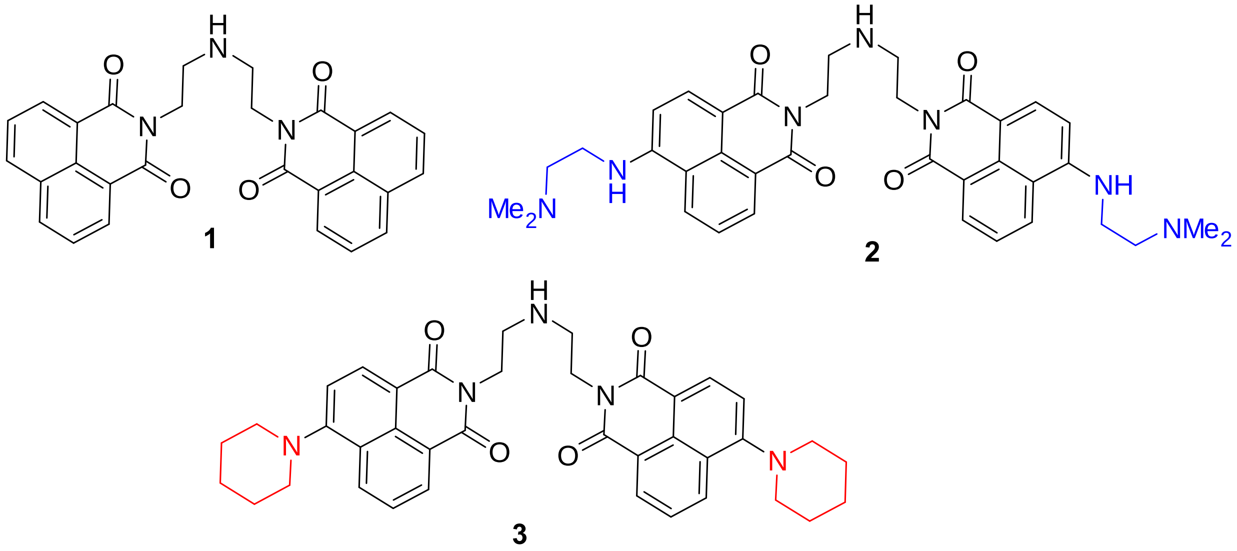
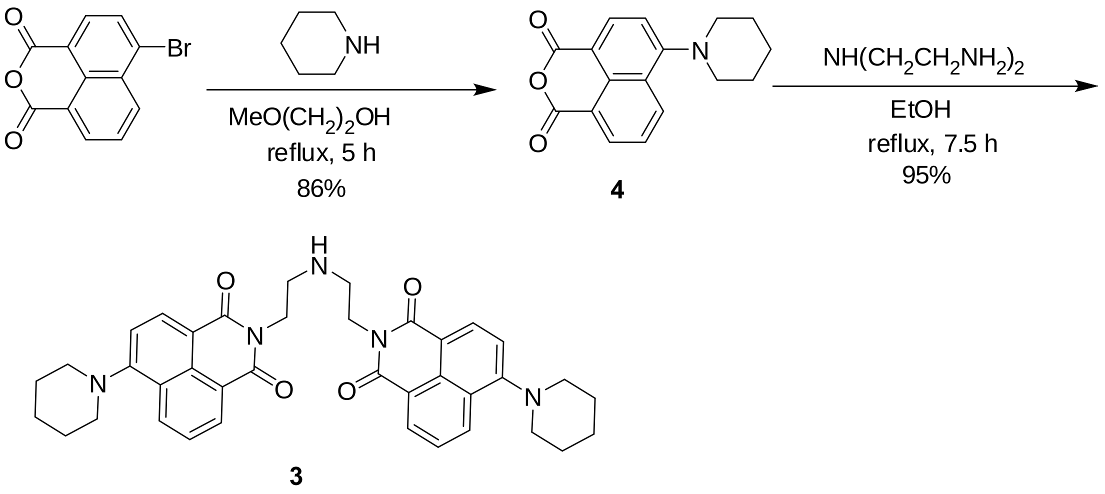


**Figure 1.** The chemical structures of bis-1,8-naphthalimide analogs **1**-**3**.

## RESULTS AND DISCUSSION

As shown in Scheme 1, 4-bromo-1,8-naphthalic anhydride firstly reacted with piperidine in 2-methoxyethanol to give 4-piperidine-1,8-naphthalic anhydride **4** in a 86% yield.[5] Then compound **3** was obtained in a 95% yield by treating compound **4** with diethylenetriamine in ethanol. The structure of compound **3** was well characterized by $^1$H NMR, $^{13}$C NMR, HR-MS and mp.



**Scheme 1.** The synthetic route of **3**

**Table 1.** Photophysical properties of **3** ($1\times10^{-6}$ M) in the presence of different solvents

| | DMF | DMSO | THF | acetone | *c*-hexane | MeCN | $CH_2Cl_2$ | MeOH |
|---|---|---|---|---|---|---|---|---|
| $\lambda_{Abs}$ (nm) | 408 | 410 | 386 | 400 | 386 | 402 | 406 | 406 |
| $A$ | 0.028 | 0.029 | 0.027 | 0.029 | 0.020 | 0.030 | 0.026 | 0.022 |
| $\lambda_F$ (nm) | 528.8 | 536 | 513.4 | 523.6 | 472.4 | 527.4 | 516 | 532.4 |
| $\Phi_F{}^a$ | 0.0118 | 0.008 | 0.300 | 0.071 | 0.144 | 0.276 | 0.431 | 0.0043 |
| $\nu_A$-$\nu_F$ ($cm^{-1}$)$^b$ | 5600 | 5730 | 6430 | 5900 | 4740 | 5910 | 5250 | 5850 |

$^a$The fluorescence quantun yields were obtained by quinine sulfate in 1 N $H_2SO_4$ ($\Phi_F$ = 0.55) as a reference; $^b\nu_A$-$\nu_F$ ($cm^{-1}$) is Stokes shift.

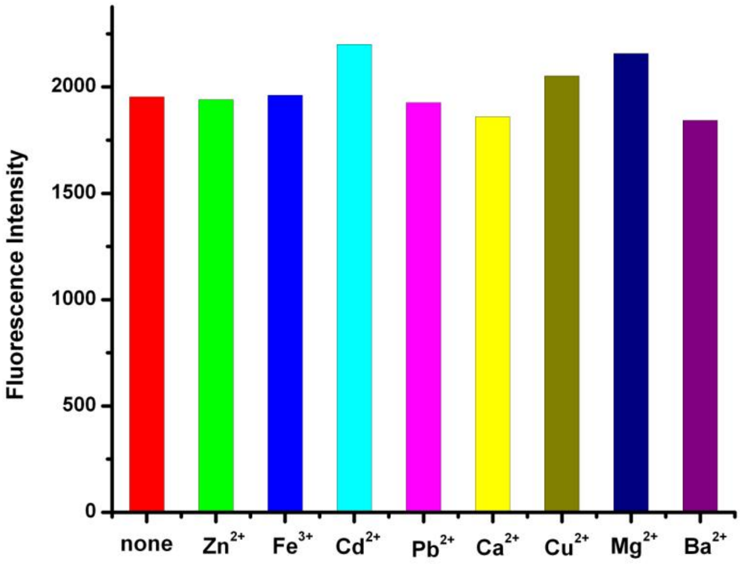


**Figure 2.** Variation of the fluorescent intensity at $\lambda_{max}$ (513 nm) of compound **3** ($1\times10^{-6}$ M) in THF in the presence of 5.0 equiv. of the respective metal cations.

The data of absorption ($\lambda_A$), fluorescence ($\lambda_F$), quantum yield of fluorescence ($\Phi_F$), and Stokes shift ($\nu_A$-$\nu_F$) of **3** in the different organic solvents were listed in Table 1. Due to the good solubility for the HTM ions and the fluorescent quantun yields ($\Phi_F$), tetrahydrofuran (THF) was chosen as the solvent for all the measurements. Firstly, the metal-induced fluorescence changes of **3** in THF solution were investigated. As shown in Figure 2, an enhancement or reducement of fluorescent intensity of **3** in the presence of different metal cations (such as $Zn^{2+}$, $Fe^{3+}$, $Cd^{2+}$, $Pb^{2+}$, $Ca^{2+}$, $Cu^{2+}$, $Mg^{2+}$, and $Ba^{2+}$) has not been observed. Then the influence of protons on the fluorescent intensity of **3** was also tested in water over a pH range of 3.04-9.34. The parameters of absorption and fluorescent spectra of **3** in water of different pH were listed in Table 2. As outlined in Figure 3, compound **3** exhibited high sensitivity to the presence of protons. For example, from pH 8.20 to 4.88, a dramatic decrease in the fluorescent intensity of **3** was observed. That is, the fluorescent intensity of **3** was greatly reduced when the solution became acidic. Meanwhile, the fluorescent intensity of **3** at pH 8.20 was more than 17 times of that at pH 3.04. It should be noteworthy that the fluorescent intensity of **3** was absolutely observed in water, while the fluorescent intensity of **1** and **2** was observed in mixture solution (*e.g.*, MeCN/$H_2O$ or MeOH/$H_2O$).[10,11] The pH dependence of fluorescent intensity could be analyzed with below equation to give the p$K_a$ value.

$$\log[(I_{Fmax} - I_F)/(I_F - I_{Fmin})] = pH - pK_a$$

**Table 2.** Parameters of absorption and fluorescent spectra of compound **3** ($1\times10^{-6}$ M)[a]

| | Compound **3** |
|---|---|
| $\lambda_{Abs}$ (pH 3.04) [nm] | 416 |
| $A$ | 0.014 |
| $\lambda_{Abs}$ (pH 8.20) [nm] | 410 |
| $A$ | 0.013 |
| $\lambda_F$ (pH 3.04) [nm] | 545.6 |
| $\Phi_F$ (pH 3.04) | 0.002969 |
| $\lambda_F$ (pH 8.20) [nm] | 531.8 |
| $\Phi_F$ (pH 8.20) | 0.021948 |
| p$K_a$ | 7.25 |

[a] Compound **3** was characterized at 288 K in water of different pH.

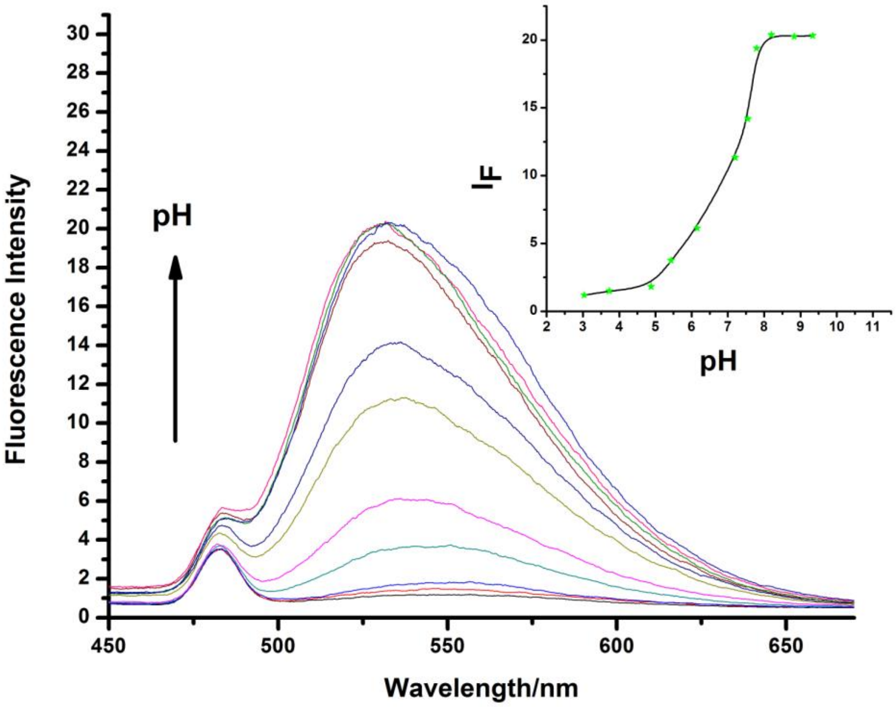


**Figure 3.** Changes in the fluorescence spectra of **3** as a function of pH in water. Inset: Fluorescence intensity of **3** *vs.* pH (pH adjusted by $HClO_4$ or $N^+Me_4OH^-$) in water.

The calculated p$K_a$ value was 7.25 (288 K). Interestingly, the influence of protons on the fluorescent intensity of **3** was completely different from its other bis-1,8-naphthalimide analogs **1** (p$K_a$ = 7.53) and **2**(p$K_a$ = 6.85).[10,11] For example, the fluorescent intensity of **3** was greatly reduced as the solution became acidic, while the fluorescent intensity of **1** and **2** were greatly reduced as the solution became alkali. The difference of the chemical structures between **3** and **1** (hydrogen atom) or **2** (*N*,*N*-dimethylaminoethylamino group) was only the different substituents on the 4-position of bis-1,8-naphthalimide. The proposed mechanism for the observed quenching process for **3** in the weakly acidic conditions was due to the formation of intramolecular hydrogen bond between the nitrogen atom of diethylenetriamine and oxygen atoms of aminonaphthalimide.

In summary, a new fluorescent chemosensor **3** based upon bis-4-piperidine-1,8-naphthalimide linked by the diethylenetriamine was synthesized, and its fluorescent properties were also investigated. Different from other bis-1,8-naphthalimides, no changes in the fluorescence spectra of **3** in the presence of metal cations was observed, and it displayed an unexpectedly strong fluorescence quench in weakly acidic aqueous solutions. It would be suited as a new pH sensor to monitor changes in the physiological pH conditions.

## EXPERIMENTAL

All solvents and reagents were used as obtained from commercial sources without further purification. The solutions of metal ions were prepared from $Zn(ClO_4)_2 \cdot 6H_2O$, $Fe(ClO_4)_2 \cdot 6H_2O$, $Ca(ClO_4)_2 \cdot 4H_2O$, $Mg(ClO_4)_2$, $Ba(ClO_4)_2$, $Pb(ClO_4)_2$, $Cd(ClO_4)_2$, and $Cu(ClO_4)_2$, respectively, and were dissolved in distilled THF. Analytical thin-layer chromatography (TLC) and preparative thin-layer chromatography (PTLC) were performed with silica gel plates using silica gel 60 $GF_{254}$ (Qingdao Haiyang Chemical Co., Ltd.). Melting points are uncorrected. Nuclear magnetic resonance spectra (NMR) were recorded on a Bruker Avance DMX 400 MHz instrument in $CDCl_3$ ($^1H$ at 400 MHz and $^{13}C$ at 100 MHz) using TMS (tetramethylsilane) as the internal standard. High-resolution mass spectra (HR-MS) and mass spectra (MS) were carried out with APEX II Bruker 4.7T AS instrument and HP 5988 instrument, respectively. All pH measurements were carried out with a pH-meter PHS-3C (Chengdu Century Fangzhou Science& technology Co., Ltd.). Fluorescent spectra were determined on a Hitachi F-4500 spectrophotometer. UV-visible spectra were determined on a Hitachi U-3310 spectrophotometer.

***Synthesis of compound 4***. A mixture of 4-bromo-1,8-naphthalic anhydride (2.77 g, 10.0 mmol), and piperidine (1.97 mL, 20 mmol) in 2-methoxyethanol (25 mL) was refluxed for 5 h, then the reaction mixture was cooled to room temperature to afford a yellow solid after filtration, which was purified by recrystallization from EtOH to give 2.41 g (86%) of **4** as the orange needles. Mp 170-171 $^oC$ (lit.,[12] 175-176 $^oC$); $^1H$-NMR (400 MHz, $CDCl_3$ ): $\delta$ 8.58 (d, $J$ = 7.6 Hz, 1H), 8.50 (d, $J$ = 8.4 Hz, 1H), 8.44 (d, $J$

= 8.8 Hz, 1H), 7.73 (t, *J* = 7.6 Hz , 1H), 7.20 (d, *J* = 8 Hz, 1H), 3.31 (t, *J* = 5.6 Hz, 4H), 1.88-1.93 (m, 4H), 1.74-1.78 (m, 2H); EI-MS m/z: 281($M^+$, 83 ), 280 ($[M-1]^+$, 100).

***Synthesis of compound 3***. A mixture of **4** (351mg, 1.25 mmol), and diethylenetriamine (0.054 mL, 0.5 mmol) in absolute EtOH (20 mL) was refluxed for 7.5 h under an argon atmosphere. After removal of EtOH, the residue was purified by preparative thin-layer chromatography (PTLC) using $CH_2Cl_2$/MeOH (20:1, v/v) as eluent to afford 299 mg (95%) of **3** as a yellow solid. Mp 115-116 $^oC$; $^1H$-NMR (400 MHz, $CDCl_3$): $\delta$ 8.28-8.37 (m, 6H), 7.60 (t, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 4.34 (t, *J* = 6.4 Hz, 4H), 3.11-3.21 (m, 12H), 2.80 (s, 1H), 1.86-1.90 (m, 8H), 1.72-1.73 (m, 4H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 164.7, 164.2, 132.5, 130.9, 130.3, 129.8, 126.1, 125.1, 122.9, 115.8, 114.5, 54.5, 47.4, 39.3, 26.2, 24.3; HRMS: Calcd. for $C_{38}H_{40}N_5O_4$ $(M+H)^+$: 630.3075. Found: 630.3083.

## ACKNOWLEDGEMENTS

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