Naphthalene Ring-Fused 2-Aminotryptanthrin as a Fluorescent Chemosensor for Al^{3+}

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Naphthalene ring-fused 2-aminotryptanthrin (**Naph-T2NH₂**) was synthesized as a fluorescent chemosensor for Al^{3+} . We investigated the metal-ion recognition of **Naph-T2NH₂** through individual addition of Mg^{2+} , Ca^{2+} , Ba^{2+} , Fe^{2+} , Fe^{3+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Ag^+ , Zn^{2+} , Cd^{2+} , Hg^{2+} , Al^{3+} , and Pb^{2+} in an acetonitrile solution. When Mg^{2+} , Ca^{2+} , Ba^{2+} , Co^{2+} , Ag^+ , Zn^{2+} , and Cd^{2+} were individually added to the solution, the shape and intensity of the fluorescence spectra did not change. Conversely, when Fe^{2+} , Fe^{3+} , Ni^{2+} , Cu^{2+} , Hg^{2+} , and Pb^{2+} were individually added to the solution, the fluorescence at 604 nm was quenched. However, the fluorescence at 494 nm increased significantly upon addition of Al^{3+} . Thus, **Naph-T2NH₂** is well suited for use as a fluorescent chemosensor for Al^{3+} .

Key words: aluminum ion, 2-aminotryptanthrin, fluorescent dye, fluorescent chemosensor

1. INTRODUCTION

Tryptanthrin (**T**, Fig. 1a) is a weakly basic alkaloid formed in a number of plant species [1] that exhibits antimicrobial activity against various pathogenic bacteria and fungi [2]. Upon synthesizing tryptanthrin derivatives as antimicrobial agents [3], some were found to be fluorescent. We have previously shown that 2-aminotryptanthrin (**T2NH₂**, Fig. 1b) has excellent photophysical properties such as a wide wavelength absorption and emission in the visible region, as well as a high fluorescence quantum yield (Φ_f) [4]. The fluorescence spectra of **T2NH₂** in various polarity solvents demonstrated large, positive fluorescent solvatochromism, indicating that **T2NH₂** exhibits a longer fluorescence wavelength in highly polar solvents compared to nonpolar solvents [5]. **T2NH₂** and its derivatives have widespread potential applications in diverse fields, such as labeling reagents, chemosensors, laser dyes, photosensitizers, and fluorescent organic devices [6]. As such, it is necessary for these dyes to absorb and emit at long wavelengths. For example, fluorescent dyes that emit at long wavelengths are desirable for applications in biological systems as they reduce auto-fluorescence and photodamage to living cells [7]. Therefore, we propose to shift the absorption maxima ($\lambda_{a, \text{max}}$) and the emission maxima ($\lambda_{f, \text{max}}$) of **T2NH₂** to longer wavelengths by expanding the π -conjugation of the aromatic rings. We synthesized naphthalene ring-fused 2-aminotryptanthrin (**Naph-T2NH₂**, Fig. 1c) and investigated the metal ion recognition of **Naph-T2NH₂** through the individual addition of Mg^{2+} , Ca^{2+} , Ba^{2+} , Fe^{2+} , Fe^{3+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Ag^+ , Zn^{2+} , Cd^{2+} , Hg^{2+} , Al^{3+} , and Pb^{2+} in an acetonitrile solution.

2. EXPERIMENTAL

2.1 Measurements

Stock solutions of **Naph-T2NH₂** were prepared by dissolving appropriate amounts of **Naph-T2NH** in acetonitrile. Titrations of **Naph-T2NH₂** ($[\text{Naph-T2NH}_2] =$

Figure 1 Structures of (a) tryptanthrin (**T**), (b) 2-aminotryptanthrin (**T2NH₂**), and (c) naphthalene ring-fused 2-aminotryptanthrin (**Naph-T2NH₂**).

10 μM , $M = \text{mol dm}^{-3}$) against metal ion solutions were performed in a spectrophotometric cell with a path length of 1 cm. UV-vis spectra (between 200 and 800 nm) of the resulting solutions were recorded at room temperature with a JASCO V-670 spectrophotometer after individual additions of each of the 14 metal salts: $\text{Mg}(\text{ClO}_4)_2$, $\text{Ca}(\text{ClO}_4)_2$, $\text{Ba}(\text{ClO}_4)_2$, $\text{Fe}(\text{ClO}_4)_2$, $\text{Fe}(\text{ClO}_4)_3$, $\text{Co}(\text{ClO}_4)_2$, $\text{Ni}(\text{ClO}_4)_2$, $\text{Cu}(\text{ClO}_4)_2$, AgClO_4 , $\text{Zn}(\text{ClO}_4)_2$, $\text{Cd}(\text{ClO}_4)_2$, $\text{Hg}(\text{ClO}_4)_2$, $\text{Al}(\text{ClO}_4)_3$, and $\text{Pb}(\text{ClO}_4)_2$. Fluorescence spectra were measured between 300 and 900 nm with a Hitachi F-4500 fluorometer using the $\lambda_{a, \text{max}}$ or the isosbestic point as the excitation wavelength (λ_{ex}). The titrations were performed with metal ions (10–10000 μM) as the titrant and **Naph-T2NH₂** (10 μM) as the titrate. The metal ion sources were identical to those used for the UV-vis studies. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a JEOL JNM-ECA 500 spectrometer in dimethyl sulfoxide ($\text{DMSO}-d_6$) with tetramethylsilane as the internal standard. High-resolution mass spectra (HRMS) were obtained using electrospray ionization (ESI) with a HITACHI NanoFrontier LD spectrometer.

2.2 Synthesis

Naph-T2NH₂ was prepared using the procedure shown in Scheme 1. A solution of diethyl ketomalonate hydrate (0.88 g, 5.8 mmol) in acetic acid (AcOH , 1.5 mL) was

Scheme 1 Synthesis of **Naph-T2NH₂**.

added over 45 min with stirring to a refluxing solution of 1-aminoanthracene (0.56 g, 2.9 mmol) in AcOH (9 mL). After addition, the reaction was refluxed for an additional 1.5 h. The AcOH was then removed in vacuo, and 10% aqueous KOH (30 mL) was added to the residue. The solution was stirred vigorously while refluxing for 4 h. After cooling, the solution was filtered to remove the small amount of solid material and carefully (due to evolution of CO₂) acidified it with 35% HCl to pH 1.0. The purple-red precipitate was filtered, washed with *n*-hexane, and dried to afford naphthalene ring-fused isatin (**Naph-Isatin**). Recrystallization in dichloromethane afford pure **Naph-Isatin** (0.21 g, 29%) [8].

SOCl₂ (0.13 mL, 1.7 mmol) was added to a solution of 2-amino-5-nitrobenzoic acid (0.062 g, 0.34 mmol) and **Naph-Isatin** (0.0083 g, 0.34 mmol) in dry pyridine (20 mL). The resulting mixture was refluxed for 1 h and then poured into ice water. The reaction mixture was extracted with dichloromethane, dried over anhydrous magnesium sulfate, and concentrated under vacuum to afford the crude product. Column chromatography on silica gel with dichloromethane as the eluent yielded pure **Naph-T2NO₂** as a purple solid (0.018 g, 13%) [9].

A mixture of **Naph-T2NO₂** (0.015 g, 0.040 mmol) and SnCl₂ · 2H₂O (0.048 g, 0.21 mmol) in tetrahydrofuran (THF, 18 mL) was refluxed for 7 h under a flow of dry nitrogen. The reaction mixture was extracted with dichloromethane, dried over anhydrous magnesium sulfate, and concentrated under vacuum to afford the crude product. Column chromatography on silica gel with dichloromethane as the eluent yielded pure **Naph-T2NH₂** as a red solid (0.0060 g, 41%) [10]. The HRMS of **Naph-T2NH₂** showed corresponding the molecular ion peaks, and the ¹H NMR spectrum confirmed that the desired compound was synthesized.

Naph-T2NH₂: ¹H NMR (500 MHz, DMSO-*d*₆) δ 6.45 (1H, s, NH₂), 7.12 (1H, dd, *J* = 2.4 Hz, 8.7 Hz), 7.56 (1H, d, *J* = 2.4 Hz), 7.73–7.61 (4H, m), 8.20–8.12 (3H, m), 8.74 (1H, s), 9.92 (1H, s); HRMS (ESI) *m/z* (M+H) calculated 364.1081, found 364.1023.

3. RESULTS AND DISCUSSION

In comparison with **T2NH₂**, **Naph-T2NH₂** exhibited red-shifted $\lambda_{a, \max}$ and $\lambda_{f, \max}$ values (476 nm and 604 nm in acetonitrile, respectively). The Φ_f values of **Naph-T2NH₂** were significantly lower than those of **T2NH₂** (0.0019 and 0.56 in acetonitrile, respectively) [11]. The molecular structures of **Naph-T2NH₂** and **T2NH₂** were calculated using density functional theory (DFT) [12]. The electron densities of the corresponding highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) surfaces of **Naph-T2NH₂** and **T2NH₂** are shown

in Fig. 2.

Figure 2 (a) Highest occupied molecular orbital (HOMO) and (b) Lowest unoccupied molecular orbital (LUMO) surfaces of **Naph-T2NH₂** and **T2NH₂** according to DFT calculations.

The strong fluorescence of **T2NH₂** can be attributed to the influence of intramolecular charge transfer (ICT) between the carbonyl group of the five-membered ring and the amino group [5]. Therefore, in **T2NH₂**, the electrons are localized on the amino group in the HOMO and on the carbonyl group of the five-membered ring in the LUMO. This is also true for the electrons in the LUMO of **Naph-T2NH₂**. However, the electrons in the HOMO of **Naph-T2NH₂** are localized on the anthracene ring. This difference in electron distribution in the HOMO could be the reason for the low Φ_f values of **Naph-T2NH₂**. That is, the fluorescence of **Naph-T2NH₂** does not have ICT characteristics. The internal conversion or the intersystem crossing could be accelerated by the difference in electron distribution in the HOMO which are localized on the anthracene ring of **Naph-T2NH₂**.

When Mg²⁺, Ca²⁺, Ba²⁺, Co²⁺, Ag⁺, Zn²⁺, and Cd²⁺ were individually added to the solution, the shape and intensity of the absorption spectra did not change, and the fluorescence spectra changed only slightly. Figure 3a shows the absorption and fluorescence spectra of **Naph-T2NH₂** with and without Ag⁺ as a typical example. Slight changes in the fluorescence spectra were most likely due to collision quenching between **Naph-T2NH₂** and the metal ions.

The addition of Fe²⁺, Fe³⁺, Ni²⁺, Cu²⁺, Hg²⁺, and Pb²⁺ to the acetonitrile solution of **Naph-T2NH₂** resulted in decreased absorption at 476 nm and observation of isosbestic points. The changes in the absorption spectra of **Naph-T2NH₂** in the presence of Fe²⁺, Fe³⁺, Ni²⁺, Cu²⁺, Hg²⁺, and Pb²⁺ suggested that Fe²⁺, Fe³⁺, Ni²⁺, Cu²⁺, Hg²⁺, and Pb²⁺ complexes were formed in the ground state. After individual addition of Fe²⁺, Fe³⁺, Ni²⁺, Cu²⁺, Hg²⁺, and Pb²⁺ to a solution of **Naph-T2NH₂**, the fluorescence at 604 nm was quenched. Figures 3b and 3c show the absorption and fluorescence spectra of **Naph-T2NH₂** with and without Hg²⁺ and Pb²⁺, respectively, as typical examples. The fluorescence at 604 nm for the **Naph-T2NH₂**–Hg²⁺

Figure 3 UV-vis absorption and fluorescence spectra of **Naph-T2NH₂** with (a) Ag^+ , (b) Hg^{2+} , (c) Pb^{2+} , and (d) Al^{3+} in acetonitrile: [**Naph-T2NH₂**] = 10 μM , Ag^+ , Hg^{2+} , Pb^{2+} , and Al^{3+} = 0–1000 equiv.

complex almost completely disappeared, while that of the **Naph-T2NH₂**– Pb^{2+} complex decreased by one third. The addition of Al^{3+} to the acetonitrile solution of **Naph-T2NH₂** resulted in a decrease in the absorption at 476 nm, along with observation of isosbestic points, as shown in Fig. 3d (left). The change in the absorption spectra of **Naph-T2NH₂** in the presence of Al^{3+} also suggested that the Al^{3+} complex was formed in the ground state. After addition of Al^{3+} to a solution of **Naph-T2NH₂**, the fluorescence at 604 nm slightly decreased and the fluorescence at 494 nm significantly enhanced, as shown in Fig. 3d (right). Fluorescence quenching occurs as a result of contamination by impurities, which leads to inaccurate results. Therefore, a fluorescence “emission” chemosensor, such as **Naph-T2NH₂**, for Al^{3+} is important. These results show that **Naph-T2NH₂** is a potential fluorescent chemosensor candidate for Al^{3+} .

4. CONCLUSION

The detection of Al^{3+} is of great interest due to its potential toxicity and widespread presence [13]. **Naph-T2NH₂** was synthesized as a fluorescent chemosensor for Al^{3+} . We investigated the metal ion recognition of **Naph-T2NH₂** through individual addition of Mg^{2+} , Ca^{2+} , Ba^{2+} , Fe^{2+} , Fe^{3+} , Ni^{2+} , Cu^{2+} , Ag^+ , Zn^{2+} , Cd^{2+} , Hg^{2+} , Al^{3+} , and Pb^{2+} in an acetonitrile solution. When

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5. ACKNOWLEDGMENTS

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