Synthesis and Metal Ion Probe Properties of Four 1,8-Naphthalimides

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Four 1,8-naphthalimide derivatives (**3a-3d**) were designed and synthesized from 1,8-naphthalic anhydride and their structures were characterized by ^{1}H NMR and MS. Their recognition ability to metal ions was then investigated. The results showed the quenching constants (K_{CV}) and binding constants (K_a) values were found in the range of 10^2-10^4 M^{-1}, indicating important metal ions recognition abilities of compounds **3a-3d**. All the compounds showed recognition of ferric ion, while compounds **3a-3d** showed the best recognition ability of silver, cadmium, ferric and ferrous ions, respectively.

Key Words: 1,8-Naphthalimides, Synthesis, Recognition, Metal ions.

INTRODUCTION

It is well known that metal ions play an important role in many foundamental physiological processes of organisms. As rich element (K, Ca, Mg, *etc.*) and trace elements (Co, Ni, *etc*) are essential elements for human body, the balance of their absorption and need do much to human's health. Whereas some metal ions, such as lead and cadmium are heavy metal pollutants, can deposit in organism body through various ways and do harm to organism body[1,2]. Therefore, it is important to effectively detect metal ions and that lead to the presence of metallic ion probes. Among many kinds of metallic ion probes, fluorescence probe which can selectively detect, signal and recognize the presence of metallic ions by the change of their fluorescence emission has attracted considerable interest[3-9]. Thus design and synthesis of novel fluorescent molecular probe had become hot subject in bioorganic chemistry.

1,8-Naphthalimides showed good fluorescence and excellent photostability, were usually introduced as fluorophore group[10,11] and widely used for high sensitivity fluorescent tracer and optical chemical sensors. So in this paper, four 1,8-naphthalimide were designed and synthesized and their metal ion recognition properties were also studied (**Scheme-I**).

EXPERIMENTAL

All reagents for synthesis were commercially available and employed as received or purified by standard methods prior to use. The ^{1}H NMR studies were carried out by the
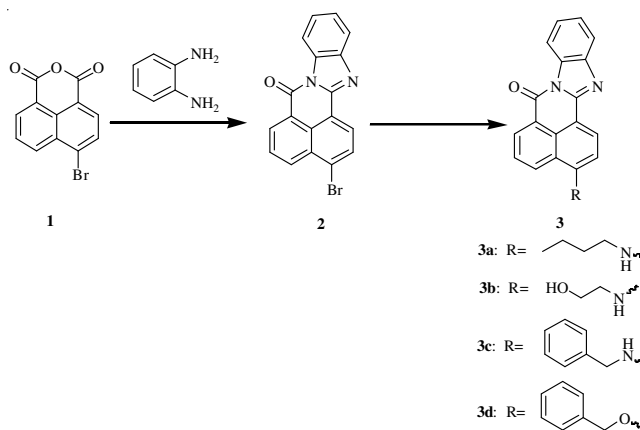
Scheme-I

BRUKER AVANCE 500 instrument and the mass spectral studies were done using BRUKER ESQUIRE HCT instrument. Melting points were recorded using an electrothermal-WRS-1A melting point apparatus and were uncorrected. UV-VIS absorption spectrums were measured in the TU-1901 spectrophotometer. Fluorescence spectra were recorded in the RF-5301 fluorospectrophotometer.

General procedure

Synthesis of compound 2: The mixture of 4-bromo-1,8-naphthalic anhydride (10 mmol) (**1**) and *o*-phenylenediamine (11 mmol) was refluxed in glacial acetic acid (50 mL) for 6 h.

Crude product was washed by anhydrous ethanol and was filtered to give compound **2** as yellow crystals.

2: Yields 87 %, ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.92 (dd, J = 7.5 Hz, 1H, ArH), 8.71 (t, J = 7.5 Hz, 1H, ArH), 8.57 (dd, J = 7.5 Hz, 2H, ArH), 8.14 (dd, J = 7.5 Hz, 1H, ArH), 7.92 (m, 2H, ArH), 7.52 (dd, J = 2.5 Hz, 2H, ArH).

Synthesis of compound 3: The mixture of compound **2** (10 mmol) and different amine or benzyl alcohol (12 mmol) was refluxed in ethylene glycol monomethyl ether (50 mL) with copper sulphate as catalyzer for 6 h, then the crude produce was purified by column chromatography to give **3** as yellow-purple crystals.

3a: Yields 70 %, m.p. 200.2-202.8 ℃, ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.87 (d, J = 5 Hz, 1H, ArH), 8..64 (d, J = 5 Hz, 1H, ArH), 8.00 (d, J = 5 Hz, 1H, ArH), 7.91(dd, J = 5 Hz, 1H, ArH), 7.69 (dd, J = 7.5 Hz, 1H, ArH), 7.48 (d, J = 5 Hz, 1H, ArH), 6.77(dd, J = 2.5 Hz, 1H, ArH), 3.42(d, J = 7.5 Hz, 2H, CH$_2$), 1.82 (q, J = 7.5 Hz, 2H, CH$_2$), 1.36-1.39 (m, J = 12.5 Hz, 1H, NH), 1.29-1.32 (m, J = 10 Hz, 4H, CH$_2$), 1.07(d, J = 7.5 Hz, 3H, CH$_3$), MS m/z (%): 342 (M + H).

3b: Yields 80 %, m.p. 230.6-232.2 ℃, ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.28 (d, J = 7.5 Hz, 1H, ArH), 8.16 (d, J = 7.5 Hz, 1H, ArH), 8.01 (d, J = 7.5 Hz, 1H, ArH), 7.64 (dd, J = 7.5 Hz, 1H, ArH), 7.59 (d, J = 7.5 Hz, 1H, ArH), 7.22 (dd, J = 7.5 Hz, 2H, ArH), 7.18 (d, J = 7.5 Hz, 1H, ArH), 4.0 (t, 1H, NH), 3.65 (s, 1H, OH), 3.58 (q, J = 7.1 Hz, 2H, CH$_2$) 3.48 (q, J = 7.1 Hz, 2H, CH$_2$). MS m/z (%): 330 (M + H).

3c: Yields 72 %, m.p. 260.1-261.8 ℃, ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.28 (d, J = 7.5 Hz, 1H, ArH), 8.16 (d, J = 7.5 Hz, 1H, ArH), 8.01 (d, J = 7.5 Hz, 1H, ArH), 7.64 (dd, J = 7.5 Hz, 1H, ArH), 7.59 (d, J = 7.5 Hz, 1H, ArH), 7.28 (d, J = 7.55 Hz, 1H, ArH), 7.22 (dd, J = 7.5 Hz, 2H, ArH), 7.20 (dd, J = 7.5 Hz, 2H, ArH), 7.18 (d, J = 7.5 Hz, 1H, ArH), 6.81 (dd, J = 7.5 Hz, 1H, ArH), 4.0 (s, 1H, NH). MS $_{m/z}$(%): 374(M-H).

3d: Yields 60 %, m.p. 270.3-272.1 ℃, ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.28 (d, J = 7.5 Hz, 1H, ArH), 8.23 (d, J = 7.5 Hz, 1H, ArH), 8.16 (d, J = 7.5 Hz, 1H, ArH), 8.01 (d, J = 7.5 Hz, 1H, ArH), 7.64 (d, J = 7.5 Hz, 1H, ArH), 7.58 (d, J = 7.5 Hz, 1H, ArH), 7.49 (d, J = 7.5 Hz, 1H, ArH), 7.42 (d, J = 7.5 Hz, 1H, ArH), 7.21 (d, J = 7.5 Hz, 1H, ArH), 7.20 (dd, J = 7.5 Hz, 2H, ArH), 7.18 (dd, J = 7.5 Hz, 1H, ArH), 6.51 (d, J = 7.5 Hz, 1H, ArH), 6.48 (d, J = 7.5 Hz, 1H, ArH), 3.52 (s, 2H, CH$_2$), 3.19 (s, 2H, CH$_2$). MS m/z (%): 377 (M + H).

Recognition ability to metal ions detected by fluorescence spectroscopy: The metallic ion recognition properties of the compounds **3** were investigated by fluorescence quenching spectroscopy. At room temperature, compounds **3** and metal ions nitrate (NaNO$_3$, KNO$_3$, Mg(NO$_3$)$_2$, Fe(NO$_3$)$_2$, Fe(NO$_3$)$_3$, Cd(NO$_3$)$_2$, Pb(NO$_3$)$_2$, Co(NO$_3$)$_2$, Cu(NO$_3$)$_2$, AgNO$_3$, Ni(NO$_3$)$_2$ and Zn(NO$_3$)$_2$) were dissolved in DMF-water (7:3, v:v) to proper concentration, respectively. The fluorescence spectroscopy was scanned in the RF-5301 fluorospectrophoto meter after mixed solution reached a steady state.

Recognition ability to metal ions confirmed by UV-visible spectrum: At room temperature, compounds **3** and metal ions nitrate [KNO$_3$ and Fe(NO$_3$)$_3$] were dissolved in DMF-water (7:3, v:v) to proper concentration, respectively. The UV-visible spectrum was scanned in the TU-1901 spectrophotometer after mixed solution reached a steady state.

Illustrated by the case of compound **3b**, the fluorescence spectra of the compound **3b** in the presence of various concentrations of metal ion was shown in Fig. 1. As shown in Fig. 1(A), it showed no recognition to Na$^+$, K$^+$, Mg^{2+}, Ni^{2+}, Cu^{2+}. And Pb^{2+}, Zn^{2+}, Fe^{2+}, Ag$^+$ had a little effect on the fluorescence of compound **3b**. The adding of Co^{2+} caused fluorescence of compound **3b** reduced without regularity, while adding of Fe^{3+}, Cd^{2+} caused fluorescence linear weak, as shown in Fig. 1(B).
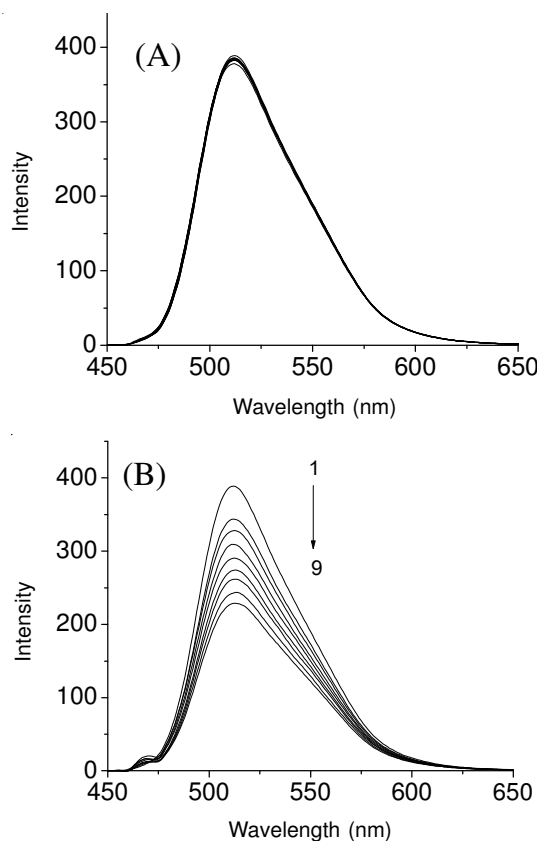

Fig. 1. Fluorescence spectra of the compound **3b** in the presence of various concentrations of sodium (A) and ferric (B) ions. The concentrations of Fe^{3+}: 1 → 9 were 0, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0 × 10^{-4} mol L^{-1}, respectively

Fluorescence quenching of compound **3** by metal ions was confirmed by the Stern-Volmer eqn.[12,13] 1 and modified Stern-Volmer eqn.[12,13] 2 as shown in Fig. 2 and the values of Stern-Volmer quenching constant (K$_{CV}$) and binding constants (K$_a$) were showed in the Tables 1 and 2, respectively.

$$\frac{F_0}{F} = 1 + K_q \, \tau_0 c(Q) = 1 + K_{cv}\, c(Q) \tag{1}$$

$$\frac{F_0}{F_0 - F} = \frac{F_0}{\Delta F} = \frac{1}{f_a K_a \, c(Q)} + \frac{1}{f_a} \tag{2}$$

As shown in Tables 1 and 2, all the compounds showed recognition to ferric ion and the quenching constant (K$_{CV}$) and binding constants (K$_a$) values were in the range of 10^2-10^3 M^{-1}. The order was: **3c > 3b > 3a > 3d**. It was possibly due to that ferric ion had strong oxidative which made the fluorescence quenching phenomenon stronger. In addition, the electron
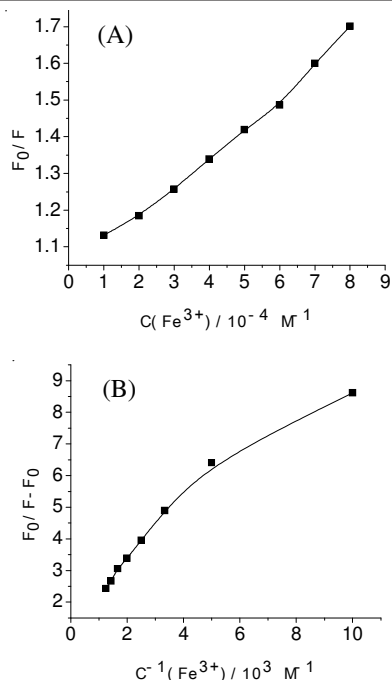
Fig. 2. Stern-volmer plots (A) and Modifed Stern-volmer plots (B) for the quenching of **3b** by ferric ion

Fig. 3. UV-VIS absorption spectra of the compound **3a** with ferric (A) and potassium (B) ions

TABLE-1
THE QUENCHING CONSTANTS OF COMPOUND **3**

Compound	$K_{CV/Fe}^{3+}$ (L mol^{-1})	$K_{CV/Fe}^{2+}$ (L mol^{-1})	$K_{CV/Ag}^{+}$ (L mol^{-1})	$K_{CV/cd}^{2+}$ (L mol^{-1})
3a	8.00×10^2	–	3.40×10^2	–
3b	8.13×10^2	–	–	2.74×10^3
3c	1.38×10^3	–	–	–
3d	2.87×10^2	3.99×10^3	–	–

TABLE-2
THE BINDING CONSTANTS OF COMPOUND **3**

Compound	$K_{a/Fe}^{3+}$ (L mol^{-1})	$K_{a/Fe}^{2+}$ (L mol^{-1})	$K_{a/Ag}^{+}$ (L mol^{-1})	$K_{a/cd}^{2+}$ (L mol^{-1})
3a	4.63×10^2	–	1.68×10^3	–
3b	1.41×10^3	–	–	8.48×10^4
3c	4.61×10^3	–	–	–
3d	3.03×10^2	2.04×10^3	–	–

donor group introduced to benzene ring can improve the electron density of coordination site, which was beneficial to the insert of ferric ion. For compound **3a**, it showed the best recognition ability to silver ion, with binding constant K_a 1.68 $\times 10^3$ M^{-1}. For compods **3b** and **3d**, they displayed the best recognition ability to cadmium ion and ferrous ion, respectively, with binding constant K_a 8.48×10^4 and 2.04×10^3 M^{-1}. For compond **3c**, it demonstrated selective recognition on ferric ion.

The UV-visible absorption spectra of the compounds **3a**-**3d** with ferric and potass ions system were also selectively measured to further confirmed the metal ions recognition. As shown in Fig. 3(A), it can be seen that the UV-visible absorption spectra **3a**-**3d** decreased as the addition of ferric ion, while that of **3a**-**3d** with potassium ion displayed no change as shown in Fig. 3(B). The phenomenon was consistent with that in fluorescence quenching spectroscopy, confirming the metal ions recognition of compounds **3a**-**3d**.
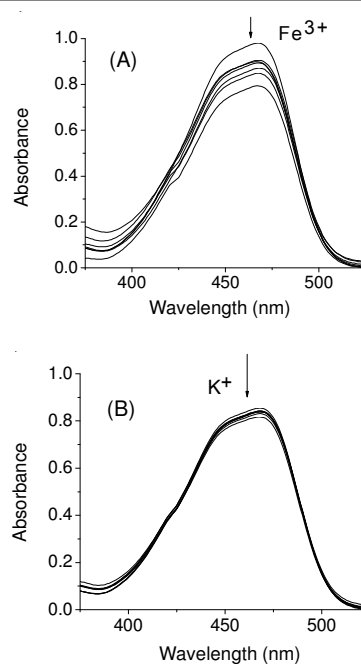
Conclusion

Four naphthalimeds **3a**-**3d** were synthesized and their metal ions recognition was evaluated. The results showed that compounds **3a**-**3d** displayed important metal ions recognition abilities.

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