#### **ORIGINAL ARTICLE**

# Dual Naked-Eye Optical Sensor Based on Imidazolium Cation and Napthalamide for Specific Detection of Fluoride

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#### Abstract



A novel naked eye fluorescence sensor (ANI) based on naphthalimide and imidazolium moieties for fluoride detection has been designed and synthesized by multiple step synthesis. The fluorescence response of ANI sensor was significantly quenched in the presence of fluoride ion upon the interaction between an acidic amide proton and acidic C2 proton (-C(2)*H*-) of imidazolium compound. The binding behavior of ANI and  $F^-$  ion was extensively explored by using NMR titration. Comparison of binding ability of ANI and AN sensors addressed the dominant electrostatic and hydrogen bonding interaction with  $F^-$  ion. Consequently, ANI sensor highlights a strong binding with  $F^-$  ions with a high selectivity over AN. Interestingly, ANI demonstrated a naked-eye response with colorimetric and fluorometric assay.

Keywords Anion recognition · Fluorescence · Fluoride anion · Dual optical sensor

# Introduction

Anion recognition and sensing has been growing fast and very attractive to supramolecular chemists due to their important roles in many fields such as biological, environmental, clinical and chemical applications [1–3]. Among several biologically related anions, fluoride is very interesting anion because fluoride plays the essential role in dental care and osteoporosis [4]. However, the high concentration of fluoride in our bodies can cause dental and skeletal fluorosis and inhibit the biosynthesis of neurotransmitters in the fetuses [5, 6]. Therefore, research which is involving the development of sensitive chemosensors for fluoride detection becomes more challenge.

Fluorescence chemosensors have been widely used for molecular and ion recognition including biological

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<sup>2</sup> School of Molecular Science and Engineering, Vidyasirimedhi Institute of Science and Technology (VISTEC), Wangchan, Rayong 21210, Thailand compounds, metal ions and various anions because of their high selectivity, high sensitivity and fast response [7-10]. Generally, the anion recognition unit usually utilizes several binding sites such as pyrrole, urea, thiourea and amide due to hydrogen bonding interactions between NH position and anions [11–14]. Moreover, electrostatic interactions would promote the anion complexation because the strength of positive charge moiety could attract anions. Interestingly, imidazole compound is a heterocyclic aromatic compound which can be protonated to form imidazolium moiety [15]. In recent years, imidazolium salts were very popular for anion detection because it can attract various anions by using their positive charge and hydrogen bonding moiety [16]. In addition, naphthalimide is a popular dye because it was easily modified with a variety of functional groups and offered strong absorption and fluorescence response [17-19]. In this work, we have designed and synthesized a novel naked-eye fluorescence sensor (methylated imidazolium, ANI) based on naphthalimide and imidazolium moieties acting as the signaling and binding sites, respectively. Owing to the photophysical properties of sensor, the ANI sensor exhibited the color and fluorescence changes in a particular of fluoride ion. As anticipated, to further develop the effectively complementary interaction for the promoting a high binding affinity by taking a benefit of positive charge and strong acidic proton on imidazolium moiety (C2), the binding ability of (nonmethylated imidazole, AN) without positive charge in its structure were clearly compared to ANI.

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# Experimental

# **General Information**

<sup>1</sup>H NMR and <sup>13</sup>C NMR were recorded on a Varian Mercury Plus 400 NMR spectrometer and Bruker Avance 400 NMR. MALDI-TOF mass spectra were recorded on Bruker Doltonic. HRMS mass spectra were recorded on Bruker Compact. Absorption spectra were recorded on a Varian Cary 50 UV-Vis spectrophotometer. All fluorescence spectra were measured by Cary Eclipse Varian fluorescence spectrophotometer. All naked-eve fluorescence photos were recorded by Samsung galaxy S5. All reagents were purchased from commercial suppliers and they were used without further purification. All commercial grade solvents were purified by distillation before used. Thin-layer chromatography (TLC) was performed on silica gel plates (Kieselgel 60 F254, 1 mm, Merck). Spectrophotometric grade dimethylsulfoxide (DMSO) used in UV-Visible and fluorescence measurement was provided from Merck.

#### Typical Procedure for the Synthesis of ANI and AN

# Synthesis of 6-Bromo-2-Phenyl-1H-Benzo[de] Isoquinoline-1,3(2H)-Dione (1)

4-Bromo-1,8-naphthalic anhydride (5 g, 18 mmol) and aniline (2 mL, 21.9 mmol) were dissolved in dried methanol. The mixture was stirred for 5 min. The catalytic amount of pyridine was added into the mixture and it was refluxed overnight under nitrogen atmosphere. Subsequently, the brownish crude product was purified by washing with methanol and dichloromethane 3 times, and recrystallized with methanol to obtain compound **1** as white solid (6.02 g, 95% yield).

<sup>1</sup>**H NMR** (400 MHz,  $d_6$ -DMSO): δ (in ppm) = 8.57 (t, J = 7.4 Hz, 2H, Ar*H*), 8.32 (d, J = 8.0 Hz, 1H, Ar*H*), 8.23 (d, J = 8.0 Hz, 1H, Ar*H*), 8.01 (t, J = 7.8 Hz, 1H, Ar*H*), 7.51 (d, J = 7.4 Hz, 2H, Ar*H*), 7.45 (d, J = 7.2 Hz, 1H, Ar*H*), 7.37 (d, J = 6.8 Hz, 2H, Ar*H*).

<sup>13</sup>C NMR (100 MHz,  $d_6$ -DMSO): δ (in ppm) = 163.14, 163.08, 135.75, 132.69, 131.57, 131.36, 130.93, 129.92, 129.15, 129.01, 128.85, 128.81, 128.75, 128.26, 123.34, 122.57.

# Synthesis of 6-((2-Aminoethyl)Amino)-2-Phenyl-1H-Benzo[de] Isoquinoline-1,3(2H)-Dione (2)

Compound 1 (2.00 g, 5.68 mmol) was dissolved in 5 mL ethylene glycol monomethyl ether (EGME) and ethylenediamine (1 mL, 14.9 mmol) was added into the solution. The mixture was refluxed for 4 h under nitrogen atmosphere. After the reaction was completed, the product was precipitated by adding ice into the mixture. The sediment

was collected and dissolved with methanol and recrystallized with dichloromethane to obtain compound 2 as yellow solid (0.56 g, 30% yield).

<sup>1</sup>**H NMR** (400 MHz,  $d_6$ -DMSO): δ (in ppm) = 8.75 (d, J = 8.8 Hz, 1H, ArH), 8.41 (d, J = 7.2 Hz, 1H, ArH), 8.24 (d, J = 8.4 Hz, 1H, ArH), 7.70 (t, J = 8.0 Hz, 1H, ArH), 7.49 (d, J = 3.6 Hz, 2H, ArH), 7.41 (d, J = 7.2 Hz, 1H, ArH), 7.28 (d, J = 6.8 Hz, 2H, ArH), 3.14 (t, 2H, CH<sub>2</sub>), 2.86 (t, J = 6.6 Hz, 2H, CH<sub>2</sub>).

<sup>13</sup>**C NMR** (100 MHz, *d*<sub>6</sub>-DMSO): δ (in ppm) = 163.99, 163.14, 150.97, 136.81, 134.25, 130.74, 129.86, 128.99, 128.86, 128.75, 128.70, 127.79, 124.19, 122.19, 120.21, 107.79, 103.88, 46.35.

# Synthesis of 2-Chloro-*N*-(2-((1,3-Dioxo-2-Phenyl-2,3 -Dihydro-1H-Benzo[de]Isoquinolin-6-yl)Amino)Ethyl)Acet amide (3)

The compound **2** (1.00 g, 3.02 mmol) and Na<sub>2</sub>CO<sub>3</sub> (1.06 g, 10 mmol) were suspended in 20 mL CH<sub>2</sub>Cl<sub>2</sub> and stirred at 0 °C for 5 min under nitrogen atmosphere. Chloroacetyl chloride (0.5 mL, 6.28 mmol) was added to the mixture solution by using the syringe and then the mixture solution was stirred overnight under nitrogen atmosphere. The reaction mixture was extracted with DI water and the organic phase was collected. The solvent was evaporated to give a crude product. The crude product was dissolved with methanol and recrystallized with dichloromethane to obtain the orange powder (0.62 g, 50% yield).

<sup>1</sup>**H NMR** (400 MHz,  $d_6$ -DMSO): δ (in ppm) = 8.65 (d, J = 8.4 Hz, 1H, Ar*H*), 8.50 (s, 1 H, Ar*H*), 8.42 (d, J = 7.2 Hz, 1H, Ar*H*), 8.24 (d, J = 8.4 Hz, 1H, Ar*H*), 7.87 (s, 1H, Ar*H*), 7.71 (t, J = 7.6 Hz, 1H, Ar*H*), 7.48 (d, J = 7.2 Hz, 2H, Ar*H*), 7.42 (d, J = 7.2 Hz, 1H, Ar*H*), 7.29 (d, J = 7.6 Hz, 2H, Ar*H*), 6.88 (d, J = 8.4 Hz, 1H, Ar*H*), 4.10 (s, 2H, C*H*<sub>2</sub>), 3.47 (t, J = 5.6 Hz, 2H, C*H*<sub>2</sub>), 3.45 (t, J = 6.0 Hz, 2H, C*H*<sub>2</sub>).

<sup>13</sup>**C** NMR (100 MHz, *d*<sub>6</sub>-DMSO): δ (in ppm) = 163.12, 150.62, 136.50, 134.15, 131.37, 131.06, 130.77, 130.32, 129.84, 129.18, 128.80, 128.69, 128.59, 128.48, 128.10, 127.80, 127.15, 126.54, 124.38, 119.37, 103.78, 53.71, 43.70, 42.61.

#### **Synthesis**

of N-(2-((1,3-Dioxo-2-Phenyl-2,3-Dihydro-1H-Benzo[de] Isoquinolin-6-yl) Amino) Ethyl)-2-(1H-Imidazol-1-yl) Acetamide (AN)

Imidazole (0.20 g, 2.94 mmol) and NaH powder in catalytic amount were dissolved in 10 mL THF at 0 °C and stirred for 15 min. The compound **3** (0.50 g, 1.22 mmol) in 15 mL of DMF/THF (1:99) mixing solvent was slightly added into the mixture solution. The reaction was stirred overnight under nitrogen atmosphere. The solvent was

removed by a rotary evaporator to give a crude product which then was extracted with  $CH_2Cl_2/H_2O$  3 times. The organic phase was collected and evaporated under vacuum to yield crude product. Then, the crude product was recrystallized with methanol to obtained the yellow solid (0.36 g, 67% yield).

**FT-IR** (ATR)  $\nu_{\text{max}}$  cm<sup>-1</sup>: 3369 (m, N-H stretching); 3291 (m, N-H stretching); 2919–2849 (m, C-H stretching); 1640 (s, C=O stretching); 1361 (s, C-H stretching); 1236 (s, aromatic); 1149 (m, C-N stretching,).

<sup>1</sup>**H NMR** (400 MHz, *d*<sub>6</sub>-DMSO): δ (in ppm) = 8.65 (d, J = 8.4 Hz, 1H, Ar*H*), 8.42 (d, J = 7.2 Hz, 1H, Ar*H*), 8.38 (s, 1H, N*H*), 8.25 (d, J = 8.4 Hz, 1H, Ar*H*), 7.88 (s, 1H, CON*H*), 7.71 (t, J = 8.0 Hz, 1H, Ar*H*), 7.56 (s, 1H, Ar*H*), 7.47 (t, J = 3.6 Hz, 2H, Ar*H*), 7.42 (t, J = 7.2 Hz, 1H, Ar*H*), 7.28 (d, J = 6.8 Hz, 2H, Ar*H*), 7.07 (s, 1H, Ar*H*), 6.87 (d, J = 8.4 Hz, 1H, Ar*H*), 6.85 (s, 2H, Ar*H*), 4.67 (s, 2H, C*H*<sub>2</sub>), 3.48 (t, J = 2.6 Hz, 2H, C*H*<sub>2</sub>), 3.43 (t, J = 5.4 Hz, 2H, C*H*<sub>2</sub>). <sup>13</sup>C NMR (100 MHz, *d*<sub>6</sub>-DMSO): δ (in ppm) = 167.55, 163.12, 150.65, 138.10, 136.50, 134.18, 130.81, 129.88, 129.18, 128.69, 128.06, 127.80, 124.40, 122.35, 120.41, 120.31, 103.77, 48.70, 42.36, 37.50.

**MALDI-TOF mass**: Anal. calcd. For  $[C_{25}H_{21}N_5O_3]^+$ m/z = 439.16, Found m/z = 439.678.

**HRMS (ESI)**: Anal. Calcd for  $[C_{25}H_{21}N_5O_3 + H]^+ m/z = 440.18$ , Found m/z = 440.1364.

#### Synthesis

# of 1-(2-((2-((1,3-Dioxo-2-Phenyl-2,3-Dihydro-1H-Benzo[de] Isoquinolin-6-yl)Amino)Ethyl)Amino)-2-Oxoethyl) -3-Methyl-1H-Imidazol-3-Ium (ANI)

Compound **AN** (0.581 g, 1.0 mmol) was dissolved in methanol. Next, methyl iodide (0.1 mL, 1.60 mmol) was slowly added into the methanol solution and then refluxed overnight at 60 °C under nitrogen atmosphere. The solution was evaporated by a rotary evaporator to give a crude product which was purified by washing with methanol 2–3 times and recrystallized with dichloromethane. The orange powder was obtained (0.18 g, 50% yield).

**FT-IR** (ATR)  $\nu_{\text{max}}$  cm<sup>-1</sup>: 3297 (m, N-H stretching), 2920–2849 (m, C-H stretching), 1639 (s, C=O stretching), 1358 (s, C-H stretching), 1232 (m, aromatic), 1145 (m, C-N stretching).

<sup>1</sup>**H NMR** (400 MHz, *d*<sub>6</sub>-DMSO): δ (in ppm) = 9.05 (s, 1H, -C(2)*H*-), 8.65 (d, *J* = 7.2 Hz, 1H, Ar*H*), 8.44 (d, *J* = 6.8 Hz, 1H, Ar*H*), 8.26 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.84 (s, 1H, CON*H*), 7.72 (t, *J* = 8.0 Hz, 1H, Ar*H*), 7.68 (s, 1H, Ar*H*), 7.65 (s, 1H, Ar*H*), 7.48 (t, *J* = 3.6 Hz, 2H, Ar*H*), 7.41 (t, *J* = 7.2 Hz, 1H, Ar*H*), 7.28 (d, *J* = 6.8 Hz, 2H, Ar*H*), 6.87 (d, *J* = 8.4 Hz, 1H, Ar*H*), 4.98 (s, 1H, C*H*<sub>2</sub>), 3.87 (s, 3H, C*H*<sub>3</sub>), 3.49 (t, *J* = 5.2 Hz, 2H, C*H*<sub>2</sub>), 3.47 (t, *J* = 4.4 Hz, 2H, C*H*<sub>2</sub>). <sup>13</sup>C NMR (100 MHz, *d*<sub>6</sub>-DMSO): δ (in ppm) = 166.22, 164.45, 163.63, 151.10,

138.19, 136.97, 134.71, 131.37, 130.38, 129.68, 129.23, 128.36, 124.96, 124.23, 123.71, 122.89, 120.84, 108.90, 104.28, 50.75, 42.75, 38.19, 36.34.

MALDI-TOF mass: Anal. calcd. For  $[C_{26}H_{23}N_5O_3]^+$ m/z = 454.19, Found m/z = 453.742. ESI-HRMS: *Anal. Calcd* for  $[C_{26}H_{24}IN_5O_3 + K]^+$  m/z = 620.06, *Found* m/z = 619.5627.

#### **Study on Complexed Properties**

The test solution was contained 10  $\mu$ M of **AN** or **ANI** sensors and 100  $\mu$ M of tetrabutyl ammonium salt of various anions including F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, Г<sup>-</sup>, CN<sup>-</sup>, OH<sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, AcO<sup>-</sup> and BzO<sup>-</sup> in DMSO solution. The reaction was stirred for 5 min prior measurement. Fluorescence spectra were recorded under the excitation at 448 nm.

# **Binding Studies**

The  $1 \times 10^{-3}$  M of **ANI** solution and  $1 \times 10^{-1}$  M stock solution of tetrabutyl ammonium fluoride was prepared in spectrophotometric grade DMSO. The test solution contained  $1 \times 10^{-5}$  M of **ANI** sensors and various amount of tetrabutyl ammonium fluoride in DMSO solution in the range of 0–5000 equiv. The 20 µL of **ANI** stock solution was pipetted into a 1-cm quartz cell and the volume of the stock solution of tetrabutyl ammonium fluoride was various added. After that, the final volume was adjusted to be 2 mL by DMSO. The reaction was stirred for 5 min prior to measurement. Fluorescence spectra were recorded under the excitation at 448 nm.

#### **NMR Titration Studies**

The  $1 \times 10^{-2}$  M of **ANI** solution and  $1 \times 10^{-2}$  M stock solution of tetrabutyl ammonium fluoride was prepared in  $d_{6^-}$  DMSO. Various amounts of F<sup>-</sup> stock solution was added into the NMR tube by micro syringe from 0 to 4 equiv. and NMR spectra were collected after each addition of F<sup>-</sup> ion. The 80 µL of **ANI** solution and varied volume of the stock solution of tetrabutyl ammonium fluoride at 80 µL, 160 µL, 240 µL and 320 µL, respectively, were prepared in the NMR tube. After that, the final volume was adjusted to be 400 µL by  $d_6$ -DMSO.

## **Naked-Eye Detection**

Typically, 10  $\mu$ M of **ANI** solution was prepared into a vial. Various amount of anion stock solution was added by a micropipette. The solution was stirred for 5 min. Finally, the solution was adjusted to be 2 mL by 100% DMSO solution. Subsequently, the solution was taken a photo with Nikon D550 camera for colorimetric assay. Moreover, the solution

was excited under UV lamp at 265 nm and taken a photo with Samsung Galaxy S5 smartphone for fluorometric assay.

# **Results and Discussion**

## Synthesis of AN and ANI Sensors

AN and ANI sensors were synthesized following to Scheme 1. They started from 4-bromo-1, 8-naphthalic anhydride to give compound 1 by using amide condensation [20, 21]. The <sup>1</sup>H-NMR spectrum showed the characteristic aromatic region around 7.20-7.50 ppm assigned to aromatic protons of aniline ring. Next, compound 1 was coupled with ethylenediamine in ethylene glycol monomethyl ether (EGME) as a solvent to obtain compound 2 [22-25]. Moreover, the ethylene protons were observed at 3.14 and 2.86 ppm which confirmed the structure of compound 2. Compound 3 was prepared from compound 2 and chloroacetyl chloride under low temperature [26]. <sup>1</sup>H-NMR spectrum showed the characteristic peaks of amide proton and aliphatic protons at 7.80 ppm and 4.10 ppm, respectively. Subsequently, compound 3 was attacked by imidazole compound under a catalytic amount of NaH to give AN sensor [15]. <sup>1</sup>H-NMR spectrum showed the new signals of imidazole moiety in the range of aromatic region. Finally, the AN sensor was methylated with methyl iodide (CH<sub>3</sub>I) to yield ANI sensor [27]. <sup>1</sup>H-NMR spectrum showed the new peaks of methyl proton at 3.87 ppm. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of compounds **1**, **2**, **3**, **AN** and **ANI**, MALDI-TOF and ESI-HRMS data of **AN** and **ANI** sensors were shown in Supporting Information.

#### Selectivity Studies of AN and ANI Sensors

The selectivity studies of **AN** and **ANI** sensors against various anions including  $F^-$ ,  $CI^-$ ,  $Br^-$ ,  $\Gamma^-$ ,  $CN^-$ ,  $OH^-$ ,  $PO_4^{3-}$ ,  $AcO^-$  and  $BzO^-$  were carried out in 100% DMSO solution. As shown in Fig. 1a, the fluorescence spectra of sensor **ANI** at 530 nm were largely quenched in the presence of 10 equiv. of  $F^-$  ion under the PET process. For the other anions, the fluorescence spectra were also slightly changed. Based on a strong base of  $F^-$ , it is possibly due to the stronger hydrogen bonding interaction between protons at amide group and  $-C(2)H^-$  signals and a electrostatic force towards  $F^-$  ion. These strong interactions induced the large fluorescence quenching.

Meanwhile, the selectivity of **AN** sensor against various anions was also determined by using fluorescence spectroscopy. The results showed that no changes of fluorescent responses were observed in the presence of any anions as shown in Fig. 1b. It suggested that **AN** sensor is unable to bind with any anions through hydrogen bonding although there are amide group in its structure. This result suggested that the positive charge and strong acid proton on C2 played a crucial role for anion binding affinity, especially  $F^-$  ion. To easily understand, the normalized fluorescence intensities (I/I<sub>0</sub>) of **ANI** and **AN** sensors with various anions were compared in the Fig. 1c. The black bar and the red bar, defined as I/I<sub>0</sub> of **ANI** and **AN** sensors, respectively, exhibited the large difference of



Scheme 1 The synthesis pathway of AN and ANI sensors: (i) pyridine, CH<sub>3</sub>OH, reflux 60 °C, (ii) EGME, reflux 120 °C, (iii) Na<sub>2</sub>CO<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C, (iv) NaH, THF, DMF, 0 °C, (v) CH<sub>3</sub>OH, reflux 60 °C



**Fig. 1** Fluorescence spectra of **a**) **ANI** sensor (10  $\mu$ M) **b**) **AN** sensor 10  $\mu$ M) and **c**) intensity bars of host (**ANI** and **AN**) upon addition of various anions including F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, CN<sup>-</sup>, OH<sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, AcO<sup>-</sup> and BzO<sup>-</sup> (10 equiv) in 100% DMSO solution ( $\lambda_{ex} = 448$  nm)

black and red bars in case of  $F^-$  anion implying that only sensor **ANI** preferentially bound with  $F^-$  ion through electrostatic interactions of the positive charge of imidazolium moiety and the additional hydrogen bonding of -C(2)*H*- and  $F^$ ion.

#### **Binding Affinities Studies**

To investigate the binding properties, the binding constant of **ANI** sensor and  $F^-$  ion was examined by fluorescence titration method. The fluorescence spectra between **ANI** sensor with various amounts of  $F^-$  ion were shown in Fig. 2. The fluorescence intensity of **ANI** sensor was gradually decreased upon the increment of  $F^-$  ion from 0 to 5000 equiv. The log  $K_s$  value of **ANI** sensor toward  $F^-$  ion was 3.05. Moreover, the stoichiometric ratio between **ANI** sensor and  $F^-$  ion was further

investigated by Job's plot analysis as shown in Fig. S15. The plot of  $(I_0-I)(1-x)$  versus mole fraction of  $F^-$  ion showed the highest point of the graph at 0.5 mol of  $F^-$  anion implying that the binding mode of **ANI** sensor and  $F^-$  ion was 1:1 stoichiometry.

Deeply understanding the binding mechanism, the <sup>1</sup>H NMR titration in  $d_6$ -DMSO was employed to verify the interaction between **ANI** sensor and F<sup>-</sup> ion. Figure 3 displayed the changes of chemical shift of **ANI** sensor in the presence of F<sup>-</sup> ion between 0 to 4.0 equiv. It showed the disappearance of the acidic amide proton (red dot) at  $\delta = 7.84$  ppm and downfield shift of -C(2)H- position (green dot) at  $\delta = 9.05$  ppm in the presence of F<sup>-</sup> ion.

Moreover, the new triplet peak at  $\delta = 16.00$  ppm was developed corresponding to the H<sub>2</sub>F<sup>+</sup> [28–30]. This species was possibly generated by the excess amount of F<sup>-</sup> ion which



**Fig. 2** a) Fluorescence spectral titration of **ANI** sensor ( $10 \,\mu$ M) in the presence of different amounts of F<sup>-</sup> ion (0-5000 equiv) in 100% DMSO solution. b) Fluorescent titration curves of **ANI** sensor in the presence of F<sup>-</sup> ion

deprotonated the acidic protons at amide position. Definitely, the observation of the downfield shift of these signals and further deprotonation upon adding excess  $F^-$  ion could confirmed that the amide proton and the acidic proton of C2 enabled to interact with  $F^-$  anion.

## **Naked Eye Detection**

For Extensive works, the use of **ANI** sensor for visual detection was examined in DMSO. Firstly, **ANI** sensor (10  $\mu$ M) was titrated with various anions including F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, Γ,



Fig. 3 NMR titration spectra of ANI sensor (100 mM) upon addition of various concentration of F<sup>-</sup> ion including 0 equiv, 0.5 equiv, 1.0 equiv, 2.0 equiv and 4.0 equiv



Fig. 4 Colorimetric assay of ANI sensor (10  $\mu$ M) responses upon addition of vary concentration (0-900 equiv) of various anions including F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, CN<sup>-</sup>, OH<sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, AcO<sup>-</sup> and BzO<sup>-</sup>

 $CN^-$ ,  $OH^-$ ,  $PO_4^{3-}$ ,  $AcO^-$  and  $BzO^-$  in the concentration range from 0 to 9.0 mM. Interestingly, the colour of **ANI** sensor was changed in the presence of  $F^-$  or  $OH^-$  ion. In the case of  $F^$ ion, the colour of **ANI** sensor was gradually changed from green to purple at the concentration of  $F^-$  ion over 200 equiv (2 mM). This phenomenon can be explained that the deprotonation of the acidic proton of **ANI** sensor by  $F^-$  ion provided the unstable intermediate species. In similar feature, the case of  $OH^-$  ion induced the gradually colour change from green to

purple at the concentration of  $OH^-$  ion over 600 equiv (6 mM). All of other anions did not induce the colour change of **ANI** sensor as shown in Fig. 4. Definitely, **ANI** sensor can be served as naked-eye detection for  $F^-$  ion at 200 equivalents (631.02 ppm) without the interference of hydroxyl anion.

Apart from the fluorescent properties of naphthalimide unit in **ANI** which performed the characteristic of a strong green brightness, the visual fluorometric assay with various anion was also investigated in DMSO.



**Fig. 5** Fluorometric assay of sensor **ANI** (10  $\mu$ M) responses upon the addition of vary concentration (0-900 equiv) of various anions including F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, CN<sup>-</sup>, OH<sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, AcO<sup>-</sup> and BzO<sup>-</sup> ( $\lambda_{exc} = 265 \text{ nm}$ )

Upon adding the various anions in concentration range from 0 to 900 equiv (0-9.0 mM.) in the ANI sensor, and exposed under UV lamp at 265 nm in the black box, the results showed that the green brightness of luminescence of ANI sensor was gradually quenched upon the addition of F ion at 200 equiv. (2 mM). Possibly, PET process occurred upon the formation of  $ANI \subset F^-$  complex. Fortunately, ANI sensor offered the benefit of the fluorometric assay of F<sup>-</sup> ion determination in the range of 200-900 equiv. (2.0-9.0 mM). On the other hand, the other anions did not exhibit the brightness changes of ANI sensor except OH<sup>-</sup> ion as shown in Fig. 5. The brightness of ANI sensor was largely decreased after adding 600 equiv. (6.0 mM) of OH ion. The excess OH ion might deprotonate the acidic proton of ANI sensor to provide the unstable complex. Therefore, ANI sensor highlighted an effectively promising selectivity for F<sup>-</sup> without the interference of OH<sup>-</sup> in the range of 2-5 mM by dual detection of colorimetric and fluorometric assays.

# Conclusion

New fluorescence sensors based on imidazole unit including AN and ANI sensors have been successfully synthesized. The fluorescence spectra of ANI sensor showed a large decrease upon binding with  $F^-$  ion. The ANI sensor forms complex with F<sup>-</sup> ion in a 1:1 stoichiometry and the log K value of this complex is 3.05. With quantitative analysis, the limit of detection and limit of quantification of ANI sensor toward F<sup>-.</sup> were 0.18 mM and 0.60 mM, respectively. According to the NMR spectrum of ANI sensor, the excess F<sup>-</sup> ion exhibited the gradual downfield shift and disappearance of amide position and the proton of H<sub>2</sub>F<sup>+</sup> appeared at 16 ppm. This result confirmed that interactions of ANI sensor and F<sup>-</sup> through the electrostatic and hydrogen bonding interactions of C2 acidic proton in the ANI sensor base. Particular in advantage of ANI sensor provided the visual determination of F<sup>-</sup> ion. ANI is the alternative candidate for detection of F<sup>-</sup> in organic solvent and further development for aqueous system is continue.

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