Synthesis, optical properties and application of a set of novel pyrazole nopinone derivatives

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Abstract

Pyrazole derivatives (**4-6**) were directly synthesized from β -pinene derivative nopinone, and they were characterized by Fourier transform infrared (FTIR) spectroscope, nuclear magnetic resonance (NMR), and mass spectrometry. Their optical properties were investigated by ultraviolet-visible spectroscopy and fluorescence spectroscopy. The three compounds emitted strong blue fluorescence in ethanol. Using a fluorescence quenching method, compound **4** could be used to detect the content (100.57%) of copper sulfate pentahydrate ($\geq 99\%$) with a RSD of 1.98%, $y = -0.1127x + 2.7148$, $R^2 = 0.9703$ (Cu^{2+} : $0.5\text{--}8.0 \times 10^{-5}$ mol/L), and compounds **4-6** also had utility of calculating the content of anhydrous ferric chloride at a wide range of concentration. Thus, compounds **4-6** are new functional fluorescents for detecting the content of some purchased products.

Keywords: Nopinone; Pyrazole derivative; Fluorescence quenching; Detection

1. Introduction

Recently, the fluorescence chemosensors for selectively detecting heavy metal ions have been paid much attention due to their potential applications [1-4]. Thus, many fluorescent compounds have been synthesized for a good detection of Cu^{2+} and Fe^{3+} ions. 3-Acetoacetyl-7-hydroxycoumarin was synthesized and used as a highly sensitive on-off fluorescent chemosensor for Cu^{2+} ion [5], while a two-photon fluorescent probe based on dansyl moiety was synthesized for detecting Cu^{2+} with a low detection limit [6]. At the same time, ethyl-2-(2-aminothiazol-4-yl)-2-(hydroxyimino)acetate was first introduced into a fluorescent probe and exhibited fluorescence enhancement for identifying Fe^{3+} ion [7], and phenanthro[9,10-*d*]imidazole-coumarin derivatives represented the selective “turn-off” fluorescence phenomenon for Fe^{3+} [8]. Furthermore, there were some new synthesized compounds with a function of detecting two ions of Cu^{2+} and Fe^{3+} , such as π -extend tetrathiafulvalene derivative [9], tetraphenylethylene based fluorescent chemosensor (RbTPE) [10], naphthalenediimide based probe [11], fluorenylidene bridged 2-naphthylamine substituted cyclotriphosphazenes [12], etc. Because of their utility, novel organic fluorescent probes for Cu^{2+} and Fe^{3+} ions are also urgently needed.

β -pinene is a main constituent of natural turpentine, and nopinone was directly obtained by oxidating β -pinene with potassium permanganate [13]. Nopinone is easy to develop new derivatives because of its C=O group [14,15], and many nopinone derivatives have been reported [16-19], such as alkylation derivatives of nopinone [20], chiral annulated indenenes [21], nopinone triazole ketones [22], pyridine derivatives of pinene [23], chiral 1,3-aminoalcohols and 1,3-diols [24], 4-pyridyl-2-aminopyrimidine derivatives [25], etc. In addition, some novel nopinone derivatives have been

synthesized for a functional application in recent years. Two useful ketene hydroxybenzylidene nopinone derivatives were provided for an application on acid-base indicator [26], and nopinone derivatives could further be used in fluorescent materials. Quinazolin-2-amine nopinone derivatives were successfully synthesized for using in cellular fluorescence imaging [27], while a novel tetrahydroquinazolin-2-amine-based high selective fluorescent sensor for Zn^{2+} was prepared from nopinone [28]. Thus, luminescent materials synthesized from nopinone have a promising potential for application, to develop more fluorescent materials based on nopinone is very meaningful for the utilization of turpentine.

In this paper, we report three novel pyrazole derivatives (**1-3**) synthesized from nopinone, and their optical properties were fully studied in the solution state. Among them, compound **1** could be used to detect Cu^{2+} and Fe^{3+} ions by using a fluorescence quenching way, and the other two were a “turn-off” fluorescence probe for Fe^{3+} ion.

Scheme 1. Synthesis of pyrazole nopinone derivatives (**4-6**)

2. Experimental

2.1. Materials and instruments

Reagents and solvents were purchased from commercial suppliers and used without further purification. All reactions were monitored by GC (America Agilent 7890A). Mass spectra were obtained on the America Agilent 5975c mass spectrometer. The ^1H and ^{13}C -NMR spectra were recorded on a Bruker AV-300 spectrometer operating at

frequencies of 300 MHz (H) and 75 MHz (C). The IR spectra ν/cm^{-1} (KBr) were recorded on Nicolet 380 FT-IR infrared spectrometer. Melting points were measured using X-6 microscopic melting point apparatus. The UV-visible absorption spectra were measured on a UV-2450 spectrophotometer (SHIMADZU) using a quartz cuvette having 1 cm path length. The fluorescence spectra were determined on a PerkinElmer LS 55 fluorescence spectrophotometer, excitation wavelength at 260 nm, scan from 300 nm to 450 nm with a 100 nm/min of scan speed. Thermal gravimetric analysis (TGA) was conducted on a Shimadzu thermal analyzer (DTG-60AH). The samples were heated under a nitrogen stream of 100 mL/min with a heating rate of 10 °C /min.

2.2. Synthesis

Compounds **1-3** were first synthesized by a condensation reaction from nopinone by a reported method [26], then compounds **4-6** were further synthesized through two steps, as shown in **Scheme 1**. These novel compounds were characterized by IR, MS, and HRMS, and these analyses confirmed compounds **4-6** to be pyrazole nopinone derivatives.

2.2.1 6,6-Dimethyl-3-(2'-hydroxyphenyl)-4,5,6,7-tetrahydro-2H-5,7-methano-indazole (4). A 250 mL dried three-necked flask equipped with a thermometer, stirrer and condenser was charged with 3-(2'-hydroxybenzylidene)nopinone **1** (5 mmol) and hydrazine hydrate (6 mmol) in 30 mL of ethanol. The resulting mixture was refluxed for 15 h until the conversion ratio of 3-(2'-hydroxybenzylidene)nopinone reached over 95% (monitored with GC). After the solvent was removed, the system was added with 1,4-dioxane (70 ml) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 5.5 mmol) to another refluxed reaction for 18 h. After adding 15 ml potassium hydroxide solution (20%) and 40 ml dichloromethane, the reacted mixture was stirred for 30 min, then it

was extracted with dichloromethane, and the organic layers were washed with saturated brine to neutrality, dried over Na₂SO₄, and concentrated to make the brown crude product, which was twice purified by recrystallization with 15 mL of ethanol. Brown crystal, yield of 52%; mp: 212.2-212.5 °C; FT-IR (KBr) ν (cm⁻¹): 3423, 3388, 2943, 2891, 1588, 1447, 1255, 752; ¹H NMR (DMSO-*d*₆, 300 MHz): 0.64 (s, 3H), 1.28-1.31 (d, 1H), 1.37 (s, 3H), 2.30 (s, 1H), 2.67-2.72 (m, 1H), 2.80-2.84 (t, 2H), 2.92-2.97 (d, 1H), 6.84-6.92 (m, 2H), 7.11-7.16 (t, 1H), 7.16-7.53 (d, 1H), 11.69 (s, 1H), 12.67 (s, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz), δ (ppm): 21.17, 25.82, 26.32, 31.87, 107.79, 116.22, 117.95, 118.89, 126.85, 128.14, 155.28; EI-MS *m/z* (%): 254 (M⁺, 83), 239 (58), 225 (14), 212 (18), 211 (100), 197 (24), 186 (27), 65 (9); HRMS (*m/z*): [M+H]⁺ calcd for C₁₆H₁₈N₂O+H⁺, 255.1491; found, 255.1493.

2.2.2 6,6-Dimethyl-3-(3'-hydroxyphenyl)-4,5,6,7-tetrahydro-2H-5,7-methano-indazole (5). A mixture of 3-(3'-hydroxybenzylidene)nopinone **2** (5 mmol), hydrazine hydrate (6 mmol), and ethanol (30 mL) was refluxed for 16 h, other conditions reference compound **4**. Yellow crystal, yield of 56%; mp: 267.2-267.4 °C; FT-IR (KBr) ν (cm⁻¹): 3426, 3286, 2981, 2944, 1621, 1571, 1225, 858, 780, 686; ¹H NMR (DMSO-*d*₆, 300 MHz): 0.65 (s, 3H), 1.25-1.28 (d, 1H), 1.38 (s, 3H), 2.29 (s, 1H), 2.67-2.72 (m, 1H), 2.75-2.93 (m, 3H), 6.69-6.72 (d, 1H), 7.11-7.13 (d, 2H), 7.19-7.24 (t, 1H), 9.48 (s, 1H), 12.31 (s, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz), δ (ppm): 21.32, 26.01, 26.09, 32.12, 111.99, 114.19, 115.84, 129.77, 157.63; EI-MS *m/z* (%): 254 (M⁺, 33), 239 (35), 225 (8), 212 (17), 211 (100), 186 (18), 65 (8); HRMS (*m/z*): [M+H]⁺ calcd for C₁₆H₁₈N₂O +H⁺, 255.1491; found, 255.1492.

2.2.3 6,6-Dimethyl-3-(4'-hydroxyphenyl)-4,5,6,7-tetrahydro-2H-5,7-methano-indazole (6). A mixture of 3-(4'-hydroxybenzylidene)nopinone **2** (5 mmol), hydrazine hydrate (6

mmol), and ethanol (30 mL) was refluxed for 18 h, other conditions reference compound **4**. Yellow powder, yield of 49%; 254.4-254.8 °C; FT-IR (KBr) ν (cm⁻¹): 3305, 2972, 2928, 1614, 1577, 1524, 1440, 1269, 1247, 839; ¹H NMR (DMSO-*d*₆, 300 MHz): 0.64 (s, 3H), 1.24-1.27 (d, 1H), 1.36 (s, 3H), 2.26 (s, 1H), 2.65-2.70 (m, 1H), 2.73-2.79 (m, 3H), 6.82-6.85 (d, 2H), 7.50-7.53 (d, 2H), 9.58 (s, 1H), 12.16 (s, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz), δ (ppm): 21.33, 25.83, 26.11, 32.11, 106.89, 115.59, 122.22, 126.41, 132.78, 156.68; EI-MS *m/z* (%): 254 (M⁺, 44), 239 (39), 225 (9), 212 (18), 211 (100), 186 (23), 65 (8); HRMS (*m/z*): [M+H]⁺ calcd for C₁₆H₁₈N₂O +H⁺, 255.1491; found, 255.1486.

3. Results and discussion

3.1 Thermal stabilities

Fig. 1. TGA thermogram of pyrazole nopinone derivatives (**4-6**).

Good thermal stability is required for fluorescent materials, so we assessed this for compounds **4-6** using TGA under a nitrogen stream (**Fig. 1**). Compounds **4-6** were thermally stable up to ca. 243 °C, 283 °C and 274 °C and at that point 5% of the material weight was lost. Among them, compound **5** had the best thermal stability. Compounds

4-6 would be further used as fluorescence materials because of their good thermal stability.

3.2 HOMO and LUMO

Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of fluorescent compounds are important for light-emitting [29-31]. The fluorescent compound is easy to lead to electron transition when the value of band gap ($\Delta E = \text{LUMO} - \text{HOMO}$) is very low. Thus, the value of ΔE was used to study fluorescence light-emitting property of compounds **4-6**, and their frontier molecular orbits had been finished by a way of computer simulation, as shown in **Fig. 2**.

Fig. 2 depicts the values of ΔE of compounds **4-6**, $6 > 5 > 4$. The pyrazole nopinone derivative with a 2'-OH group had the lowest ΔE value of 4.814 eV, while another compound of 4'-OH gave a high ΔE value of 5.138 eV. Comparing the structures of three compounds, only the position of $-\text{OH}$ was different, that was to say that ΔE was connected with the position of $-\text{OH}$. The results showed that compound **4** was easy to make electron transition and emit fluorescence in compared with the other two.

Fig. 2. Molecular orbital diagrams of HOMO and LUMO of compounds **4-6**.

3.3. Optical properties

3.3.1. Fluorescence properties in different solvents

In the solution state, the fluorescence intensity is connected with solvent, and the three pyrazole derivatives (**4-6**) were readily soluble in some solvents, such as methanol, ethanol, isopropanol, ethyl acetate, trichloromethane, dichloromethane, toluene, cyclohexane, etc. Keeping the concentration at 1.0×10^{-4} mol/L, the fluorescence spectra of compound **4** (**5** or **6**) in these solvents were also provided (**Fig. S1**, Supplementary data).

As shown in **Fig. S1a**, the fluorescence intensity of compound **4** was greatly affected by solvents, and it had better fluorescence after dissolution in methanol, ethanol, isopropanol or cyclohexane. Among them, compound **4** with methanol had the best fluorescence intensity. When compound **4** was respectively dissolved in dichloromethane and ethyl acetate, an obvious fluorescence quenching had happened. In addition, there was nearly no fluorescence of compound **4** in trichloromethane or toluene. **Fig. S1b** depicts the fluorescence spectra of compound **5** in different solvents, and the results showed that the fluorescence intensity was also concerned with the solvent. The fluorescence intensity was good and did not change when compound **5** was separately dissolved in methanol, ethanol and isopropanol. When compound **5** was dissolved in cyclohexane, ethyl acetate and dichloromethane in turn, the fluorescence intensity decreased gradually. In compared with compound **4**, the solution of compound **5** in trichloromethane only had a weak fluorescence, and the fluorescence intensity was near to zero with toluene as solvent. From **Fig. S1c**, it was concluded that the solvent affected fluorescence of compound **6** a lot. These solvents, such as methanol, ethanol, isopropanol and cyclohexane, could enhance fluorescence and provided a good intensity, and the best solvent was ethanol. An obvious fluorescence quenching of compound **6** had happened after dissolving in ethyl acetate, while it quenched again and had a wide

peak band when compound **6** was dissolved in dichloromethane. Fluorescence of compound **6** disappeared when trichloromethane or toluene was used as solvent. The results showed that the fluorescence intensity of compounds **4-6** was affected greatly by the solvent, and methanol, ethanol and isopropanol were suitable for using as solvents of the three compounds.

3.3.2. Fluorescence properties in different concentrations

The solution's concentration is also important for fluorescence light-emitting, so the fluorescence spectra of compounds **4-6** in ethanol ($2\text{-}20\times 10^{-5}$ mol/L) were fully studied, the results were shown in **Fig. 3**.

Fig. 3. Fluorescence spectra of compounds **4-6** in ethanol with different concentrations ($\lambda_{\text{ex}}=260$ nm).

As shown in **Fig. 3a** and **Fig. 3d**, the fluorescence intensity of compound **4** increased to a maximum (738.56) at the concentration of 8.0×10^{-5} mol/L, then gradually decreased,

with an increasing concentration from 10.0×10^{-5} to 20.0×10^{-5} mol/L. At the same concentration range of 2.0×10^{-5} – 20.0×10^{-5} mol/L, the changes of fluorescence intensity of compounds **5** and **6** agreed with that of compound **4**, differently, compound **5** or **6** had a maximal intensity of 862.80 or 616.27 at 6.0×10^{-5} mol/L or 4.0×10^{-5} mol/L respectively (**Fig. 3b, 3c and 3d**). It was concluded that the solution's concentration of compounds **4-6** affected fluorescence intensity a lot. After that, three fluorescence photographs of the three compounds in ethanol (1.0×10^{-4} mol/L) were further provided (**Fig. 3d**), compounds **4-6** all had good light-emitting property and emitted strong blue light. The pyrazole derivative with a 3'-OH had the best fluorescence intensity while a 4'-OH compound gave the worst intensity in the solution state.

3.3.3. Effect on acid-base

Fig. 4. Fluorescence spectral changes of compound **4** in ethanol with different molar ratios of TFA and potassium *tert*-butoxide ($\lambda_{\text{ex}}=260$ nm).

Pyrazole nopinone derivatives have -NH_2 and -OH groups, which are easy to be affected by acids and alkali, so fluorescence spectra of compounds **4-6** in ethanol (1.0×10^{-4} mol/L) affected by trifluoroacetic acid (TFA) and potassium *tert*-butoxide were finished for a further study (**Fig. 4, 5, 6**).

Fig. 4a and **4b** depict the fluorescence spectra of compound **4** with different amount of TFA, and the fluorescence gradually quenched with an increased amount of TFA. The fluorescence intensity dropped quickly when 0.5-2 equiv of TFA was gradually added to the solution, then decreased slowly when TFA was continuously added. The results showed that the addition of TFA could quench fluorescence of compound **4** in the solution state, more TFA led to more fluorescence quenching. From **Fig. 4c** and **4d**, it was clear to see that potassium *tert*-butoxide could make a significant changes of fluorescence spectra of compound **4** in ethanol. Without potassium *tert*-butoxide, a peak with high intensity appeared at 328 nm, but the intensity decreased when the solution was gradually added an enhanced potassium *tert*-butoxide, and it quenched fully with more than 4.0 equiv of potassium *tert*-butoxide added. At the same time, there was a rised intensity appeared at 380 nm when the solution of compound **4** was also in the presence of equal potassium *tert*-butoxide. When the concentration of potassium *tert*-butoxide was added to 2.0×10^{-4} mol/L, an obvious peak appeared at 380 nm with good fluorescence intensity. After that, the fluorescence intensity (380 nm) enhanced to a maximal step by step with an increasing amount of organic alkali until 8.0 equiv was added. Finally, potassium *tert*-butoxide enhanced fluorescence intensity at 380 nm, which was more than the intensiy at 328 nm. It was concluded that a large number of potassium *tert*-butoxide could quench fluorescene at 328 nm and enhanced fluorescene at 380 nm.

Fig. 5. Fluorescence spectral changes of compound **5** in ethanol with different molar ratios of TFA and potassium *tert*-butoxide ($\lambda_{\text{ex}}=260$ nm).

As shown in **Fig. 5a** and **5b**, the compound **5**'s results affected by TFA agreed with that of compound **4**, the fluorescence intensity gradually cut down with a rising TFA. That was to say that much TFA could quench fluorescence of compound **5** in ethanol. The fluorescence intensity (326 nm) reduced gradually with an increased potassium *tert*-butoxide, it agreed with that of compound **4**. However, the addition of potassium *tert*-butoxide could not enhance fluorescence intensity of compound **5** in solution, which was different from that of compound **4**. Although a new peak with slight intensity appeared at 387 nm when 4.0 equiv of potassium *tert*-butoxide was added, there was no obvious fluorescence enhancement happened. It was concluded that the addition of TFA or potassium *tert*-butoxide could lead to fluorescence quenching of compound **5** in the solution state.

Fig. 6. Fluorescence spectral changes of compound **6** in ethanol with different molar ratios of TFA and potassium *tert*-butoxide ($\lambda_{\text{ex}}=260$ nm).

Fig. 6a and **6b** depict the fluorescence spectra of compound **6** affected by TFA, which did not agree with that of compound **4** and **5**. The fluorescence intensity of 328 nm peak gradually decreased when TFA was continuously added to compound **6**'s solution, but it reduced more slowly than that of the other two. There were two peaks appeared at 328 nm and 374 nm when the molar ratio of TFA and compound **6** was 2:1. When the molar ratio of TFA and compound **6** increased to 4:1, the two peaks were very clear, and the intensity (374 nm) was more strong than that of 328 nm peak. The continuous addition of TFA led to an decrease of fluorescence intensity at 328 nm peak, while it enhanced fluorescence at 374 nm peak. The intensity (374 nm) was more than that of compound **6**'s solution without TFA when more than 16 equiv of TFA was added. The reason was that N atom of compound **4** had basicity and was easy to make

protonation after adding some TFA, which agreed with that of a benzoxazole derivative (BVDA) [32]. The results revealed that a lot of TFA could enhance fluorescence of compound **6** in the solution state. From **Fig. 6c** and **6d**, it could be seen that the fluorescence spectra affected by potassium *tert*-butoxide agreed with that of compound **4**. The fluorescence intensity (328 nm) quenched gradually when the light-emitting system was added with an increasing potassium *tert*-butoxide. A new peak appeared at 375 nm when the molar ratio of potassium *tert*-butoxide and compound **6** was 2:1, and the intensity increased with a rising amount of potassium *tert*-butoxide. With 8 equiv of potassium *tert*-butoxide added, the solution's fluorescence intensity (375 nm) was more than that of no potassium *tert*-butoxide. It told that the addition of TFA or potassium *tert*-butoxide led to a red-shift from 328 nm to 374 nm or 375 nm. It also told that much TFA or potassium *tert*-butoxide could enhance fluorescence of compound **6** in ethanol.

The results showed that the addition of TFA or potassium *tert*-butoxide could significantly change the fluorescence spectra of compounds **4-6**. The reason for quenching fluorescence by TFA might be a collision with H^+ (a proton transfer reaction in the excited state) [33]. The $-OH$ group in compounds **4** and **6** could easily response with OH^- of potassium *tert*-butoxide, and deprotonation occurred and led to a fluorescence enhancement [26].

3.3.4. Spectral responses with metal ion

In the solution state, pyrazole nopinone derivatives (**4-6**) had good fluorescence light-emitting function, and their $-NH_2$ and $-OH$ groups could response with some metal ions, then led to a fluorescence enhancement or quenching with a function of detecting metal ion. Thus, alkali metal ions and transition metal ions were used to study the spectral responses of compounds **4-6** (1×10^{-4} mol/L), UV-visible absorption and fluorescence

spectra were obtained after adding 1.0 equivalent of each metal ion, the results were shown in **Fig. S2** and **Fig. 7**.

Fig. 7. Fluorescence intensity of compounds **4** (a), **5** (b) and **6** (c) in ethanol solution with equal different metal ions ($\lambda_{\text{ex}}=260$ nm).

As shown in **Fig. S2a**, there was an obvious changes of UV-visible absorption spectra after adding Cu²⁺ or Fe³⁺, that was to say that a response had happened between compound **4** and Cu²⁺ or Fe³⁺. **Fig. 7a** showed the fluorescence intensity of compound **4** in ethanol with different metal ions, and it was clear to see that the addition of Cu²⁺ or Fe³⁺ could make a significant fluorescence quenching, and Cu²⁺ ion quenched almost totally. It told that compound **4** had a response with Cu²⁺ or Fe³⁺, which agreed with that of **Fig. S2a**. The results showed that a fluorescence quenching method of compound **4** could be further used to detect Cu²⁺ or Fe³⁺. Compared with other methods, fluorescence

quenching method is of various advantages. It is sensitive and easy and has a short analysis time [34-38].

Fig. S2b and **Fig. 7b** showed a response of UV-visible absorption and fluorescence spectra with one metal ion. A significant change of UV-visible absorption spectra occurred when compound **5**'s solution was added equal Fe^{3+} ion (**Fig. S2b**), meanwhile, the addition of Fe^{3+} also decreased fluorescence intensity significantly (**Fig. 7b**). That was to say that only Fe^{3+} ion could easily interact with compound **5**. As shown in **Fig. S2c**, the UV-visible absorption spectra of compound **6** was greatly affected by Fe^{3+} ion with its absorbance enhanced, which agreed with that of **Fig. S2a** and **Fig. S2b**. After analyzing **Fig. 7c**, the results of compound **6** affected by 11 metal ions were in accord with that of **Fig. 7b**, only Fe^{3+} ion could clearly quench fluorescence of compound **6**.

In a solution state, Cu^{2+} ion had a function of quenching fluorescence of compound **6** and Fe^{3+} ion could significantly quench fluorescence of compounds **4-6**. Comparing the structure of three compounds, only the position of $-\text{OH}$ group changed. The $-\text{NH}_2$ and $-\text{OH}$ of compound **4** was very near and easy to lead to an intramolecular interaction with a metal ion, and the $-\text{OH}$ of compound **6** was far away from $-\text{NH}_2$ and impossible to make an intramolecular interaction. Thus, it was concluded that the response of compound **4** with Cu^{2+} ion might be intramolecular interaction, and another response of compound **4** (**5** or **6**) with Fe^{3+} ion might be intermolecular interaction.

3.3.5. Linearity

To obtain a linear relation of compound **4** toward different concentrations of Cu^{2+} or Fe^{3+} for detecting the content of Cu^{2+} or Fe^{3+} in solution, we measured fluorescence spectra of compound **4** (1×10^{-4} mol/L) in ethanol upon addition of various concentrations of Cu^{2+} or Fe^{3+} ion, as shown in **Fig. 8a** or **8c**.

Fig. 8. Fluorescence spectral changes of compound **4** with different concentration of Cu^{2+} (a) and Fe^{3+} (c); The linear relationship between fluorescence intensity of compound **4** and Cu^{2+} (b) and Fe^{3+} (d) concentrations, ($\lambda_{\text{ex}}=260$ nm).

The fluorescence intensity of compound **4**'s solution decreased gradually with an increasing Cu^{2+} or Fe^{3+} ion. A relationship of peak fluorescence intensity and Cu^{2+} concentration was also provided in **Fig. S3**. Furthermore, the linear relationship of Log F and Cu^{2+} concentration ($0.05\text{--}0.8 \times 10^{-4}$ mol/L) was also finished (**Fig. 8b**), $\text{Log } y = -0.1127x + 2.7148$, $R^2 = 0.9703$. At the same time, **Fig. S4a** clearly depicted the relationship of peak intensity and Fe^{3+} concentration, and the linear relationship of intensity and Fe^{3+} concentration ($0.2\text{--}1.2 \times 10^{-4}$ mol/L) was further provided in **Fig. 8d**, $y = -27.626x + 587.95$, $R^2 = 0.9773$.

Fig. 9. Fluorescence spectral changes of compounds **5** (a) and **6** (c) with different concentration of Fe^{3+} ; The linear relationship between fluorescence intensity of compound **5** (b) or **6** (d) and Fe^{3+} concentrations, ($\lambda_{\text{ex}}=260 \text{ nm}$).

Fe^{3+} ion also had a function of quenching fluorescence of compound **5** or **6**, so their fluorescence spectra with addition of different amount of Fe^{3+} ion had been fully studied for an application on determination of the content of Fe^{3+} (**Fig. 9a** and **9c**). The peak intensity of compound **5** or **6** reduced gradually with an rising Fe^{3+} concentration, the results were clearly and respectively shown in **Fig. S4b** and **S4c**. After dealing with the data of **Fig. S4b** and **S4c**, a linear relation of intensity of compound **5** or **6** and Fe^{3+} concentration was provided in **Fig. 9b** or **9d**, compound **5**: $y = -31.234x + 747.33$, $R^2 = 0.9774$ (Fe^{3+} : $0.2\text{--}1.2 \times 10^{-4} \text{ mol/L}$); compound **6**: $y = -20.463x + 510.92$, $R^2 = 0.9788$ (Fe^{3+} : $0.2\text{--}1.0 \times 10^{-4} \text{ mol/L}$).

In conclusion, compound **4** was a fluorescence probe for detecting the content of Cu^{2+} or Fe^{3+} in ethanol with a wide range, while compounds **5** and **6** could be used to know the concentration of Fe^{3+} ion by a fluorescence quenching method in a wide range.

3.3.6. Determination of the content

In order to make use of compounds **4-6**, the contents of copper sulfate pentahydrate and anhydrous ferric chloride (purchased from the supplier) were detected for a further study, the results were shown in **Table S1** and **Table 1**. The content was calculated after measuring the peak fluorescence intensity of each sample. The measured content of copper sulfate pentahydrate was 100.57% ($\geq 99\%$) with a RSD of 1.98%, and anhydrous ferric chloride was detected to provide contents of 98.56% (compound **1**), 97.57% (compound **2**) and 98.75% (compound **3**). The linear relationships of three compounds were successfully used to measure the content of some products.

Table 1 Determination of the content.

Compound	Sample for detection	Content found (%)	Average (%)	RSD (%)
4	Copper sulfate pentahydrate	101.97	100.57	1.98
	($\geq 99\%$)	99.16		
	Anhydrous ferric chloride	97.95	98.56	0.88
	($\geq 97\%$)	99.17		
5	Anhydrous ferric chloride	97.07	97.57	0.73
	($\geq 97\%$)	98.07		
6	Anhydrous ferric chloride	98.21	98.75	0.77
	($\geq 97\%$)	99.29		

4. Conclusion

Pyrazole derivatives (**4-6**) were successfully synthesized from nopinone, and their optical properties were further studied. Compounds **4-6** exhibited fluorescence enhancement phenomenon and emitted strong blue light in ethanol. The addition of TFA could enhance fluorescence of compound **6** at 374 nm, and it increased the fluorescence intensity when the solution of compound **4** or **6** was added with much potassium *tert*-butoxide. In a solution state, Cu^{2+} ion could lead to a significant fluorescence quenching of compound **4**, while Fe^{3+} ion could quench fluorescence of compounds **4-6** respectively. A good linear relationship was obtained that compound **4** could detect the content of Cu^{2+} from 0.5 to 8.0×10^{-5} mol/L ($y = -0.1127x + 2.7148$, $R^2 = 0.9703$). At the same time, compounds **4-6** also had a function of detecting Fe^{3+} concentration at a wide range. Then the three fluorescent compounds were separately used to detect the content of copper sulfate pentahydrate or anhydrous ferric chloride for a better results. These properties make the new functional nopinone derivatives very competitive emitters for fluorescence detection, and it promotes the value of turpentine.

Acknowledgements

The authors gratefully acknowledge the project supported by the University Science Research Project of Jiangsu Province (14KJA220001), and the Committee of National Science Foundation of China (Grant No. 31470592).

References

- [1] Y. Wang, H.Q. Chang, W.N. Wu, X.L. Zhao, Y. Yang, Z.Q. Xu, Z.H. Xu, L. Jia, *Sensor. Actuat. B Chem.* 239 (2017) 60-68.
- [2] Y. Hu, F. Zhao, S.L. Hu, Y.Y. Dong, D.Z. Li, Z.H. Su, *J. Photochem. Photobio. Achem.* 332 (2017) 351-356.
- [3] P.A. More, G.S. Shankarling, *Sensor. Actuat. B Chem.* 241 (2017) 552-559.
- [4] M.M. Yu, W.W. Du, W. Zhou, H.X. Li, C.X. Liu, L.H. Wei, Z.X. Li, H.Y. Zhang, *Dyes Pigments* 126 (2016) 279-285.
- [5] H.Q. Chang, X.L. Zhao, W.N. Wu, L. Jia, Y. Wang, *J. Lumin.* 182 (2017) 268-273.
- [6] H.E. Jiang, Z.J. Li, Y.F. Kang, L.P. Ding, S. Qiao, S.T. Jia, W.F. Luo, W.S. Liu, *Sensor. Actuat. B Chem.* 242 (2017) 112-117.
- [7] Y. Wang, Z. Liu, J.H. Sun, X.G. Liu, M.S. Pei, G.Y. Zhang, *J. Photochem. Photobio. Achem.* 332 (2017) 515-520.
- [8] B. Zhao, T. Liu, Y. Fang, L.Y. Wang, B. Song, Q.G. Deng, *Tetrahedron Lett.* 57 (2016) 4417-4423.
- [9] Y.W. Ma, T.H. Leng, Y.R. Qu, C.Y. Wang, Y.J. Shen, W.H. Zhu, *Tetrahedron* 73 (2016) 14-20.
- [10] Y. Yang, C.Y. Gao, N. Zhang, D.W. Dong, *Sensor. Actuat. B Chem.* 222 (2016) 741-746.
- [11] N.V. Ghule, R.S. Bhosale, A.L. Puyad, S.V. Bhosale, S.V. Bhosale, *Sensor. Actuat. B Chem.* 227 (2016) 17-23.
- [12] E. Şenkuytu, E.T. Eçik, M. Durmuş, G.Y. Çiftçi, *Polyhedron* 101 (2015) 223-229.
- [13] B. Liu, W.W. Ao, Y. Yang, S.F. Wang, *J. Nanjing Forest. Univ.* 34 (2010) 89-94.
- [14] T. Szuppa, A. Stolle, B. Ondruschka, W. Hopfe, *Chem. Sus. Chem.* 3 (2010) 1181-1191.
- [15] A. Stolle, *Eur. J. Org. Chem.* 44 (2013) 2265-2278.
- [16] M. Kato, M. Watanabe, B. Vogler, Y. Tooyama, A. Yoshikoshi, *J. Chem. Soc. Chem. Commun.* 23 (1990) 1706-1707.
- [17] M. Watanabe, B.Z. Awen, M. Kato, *J. Org. Chem.* 58 (1993) 3923-3927.
- [18] C.T. Goralski, W. Chrisman, D.L. Hasha, L.W. Nicholson, P.R. Rudolf, D. Zakett, B. Singaram, *Tetrahedron- Asymmetr.* 8 (1997) 3863-3871.
- [19] E. Mena, P. Van De Witte, *J. Lub, Liq. Cryst.* 27 (2000) 929-933.
- [20] K.R. Campos, S. Lee, M. Journet, J.J. Kowal, D. Cai, R.D. Larsen, P.J. Reider, *Tetrahedron Lett.* 43 (2002) 6957-6959.

- [21] R.L. Halterman, L.D. Crow, *Tetrahedron Lett.* 44 (2003) 2907-2909.
- [22] R.C. da Silva Junior, V.F. Ferreira, S. Pinheiro, *Tetrahedron-Asymmetr.* 15 (2004) 3719-3722.
- [23] A.V. Malkov, A.J.P. Stewart-Liddon, F. Teplý, L. Kober, K.W. Muir, D. Haigh, P. Kočovský, *Tetrahedron* 64 (2008) 4011-4025.
- [24] Z. Szakonyi, T. Gonda, S.B. Oetvoes, F. Fueleop, *Tetrahedron-Asymmetr.* 25 (2014) 1138-1145.
- [25] Q. Zhang, Z.B. Ding, N. Sun, X. Xu, C.F. Gao, S.F. Wang, *J. Forest. Eng.* 2 (2017) 51-56.
- [26] J.L. Yang, X. Xu, Y.Q. Yang, J. Rui, Y. Zhang, H.B. Kuang, S.F. Wang, L.R. Wu, *RSC Adv.* 6 (2016) 111760-111766.
- [27] J.L. Yang, H.J. Xu, X. Xu, J. Rui, X.Y. Fang, X.Q. Cao, S.F. Wang, *Dyes Pigments* 128 (2016) 75-83.
- [28] J.L. Yang, H. Fang, X.Y. Fang, X. Xu, Y.Q. Yang, J. Rui, C.L. Wu, S.F. Wang, H.J. Xu, *Tetrahedron* 72 (2016) 4503-4509.
- [29] F.I. Wu, P.I. Shih, M.C. Yuan, A.K. Dixit, C.F. Shu, Z.M. Chung, E.W.G. Diau, *J. Mater. Chem.* 15 (2005) 4753-4760.
- [30] W. Wan, H. Du, J. Wang, Y. Le, H. Jiang, H. Chen, S. Zhu, J. Hao, *Dyes Pigments* 96 (2013) 642-652.
- [31] F. Xu, H. Wang, X. Du, W. Wang, D.E. Wang, S. Chen, X. Han, N. Li, M.S. Yuan, J. Wang, *Dyes Pigments* 129 (2016) 121-128.
- [32] P. Xue, B. Yao, J. Sun, Z. Zhang, K. Li, B. Liu, R. Lu, *Dyes Pigments* 112 (2015) 255-261.
- [33] A.G. Bracamonte, A.V. Veglia, *J. Photoch. Photobio. Achem.* 261 (2013) 20-25.
- [34] O. Duman, S. Tunc, B.K. Bozoglan, *Journal of Fluoresc.* 23 (2013) 659-669.
- [35] S. Tunc, A. Cetinkaya, O. Duman, *J. Photochem. Photobiol. B* 120 (2013) 59-65.
- [36] B.K. Bozoglan, S. Tunc, O. Duman, *J. Lumin.* 155 (2014) 198-204.
- [37] S. Tunc, O. Duman, I. Soylu, B.K. Bozoglan, *J. Lumin.* 151 (2014) 22-28.
- [38] S. Tunc, O. Duman, I. Soylu, B.K. Bozoglan, *J. Hazard. Mater.* 273 (2014) 36-43.

Graphical Abstract:

Synthesis, optical properties and application of a set of novel pyrazole nopinone derivatives

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