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Two D- π -A type fluorescent probes based on isolongifolanone for sensing acidic pH with large Stokes shifts



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A R T I C L E I N F O

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ABSTRACT

Two novel isolongifolanone derivatives (**2**–**3**) with D- π -A configuration, which had a *N*,*N*-dimethylaniline unit attached to pyrazole and pyrimidine cores, were synthesized and characterized by IR, NMR and HRMS. As the protonation of the nitrogen atoms, the probes **2**–**3** displayed the significant pHdependent spectral properties. The probe **2** exhibited a remarkable ratiometric fluorescence emission (I_{445}/I_{373}) characteristic with pK_a 2.59 and the linear response over the extremely acidic range of 1.5–4.0. The probe **3** showed an obvious emission quenching at 434 nm (λ_{ex} = 300 nm) with a pK_a of 3.69 and responded linearly to monitor the pH fluctuations with the weakly acidic range of 3.5–7.0, while exhibited a linear emission enhancement at 519 nm (λ_{ex} = 425 nm) over the extremely acidic range of 1.0 –3.5. These pH probes also displayed favorable features including large Stokes shift under acidic conditions, high selectivity, rapid response, excellent photostability and good reversibility for sensing acidic pH which were further applied to response to acidic solid and gas phase using their solid-state samples, causing dramatic fluorescence color changes. In addition, the logic gates for probe **2** were constructed to develop its potential for practical applications.

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1. Introduction

In recent years, small organic molecular materials have attracted considerable interest in the field of environmental analysis owing to their accurate and real-time responses to surroundings alterations.^{1–9} pH parameter plays a significant role in many chemical and physiological processes. The indication of the pH value is extremely essential to study the regulation mechanism.^{10,11} Compared to the traditional analytical techniques, fluorescent probes are more desirable to detect pH value due to their high selectivity and sensitivity, non-invasive detection, rapid response, simple operation and extreme signal-to-noise ratio.^{12,13} So far, an increasing number of specific and sensitive pH fluorescent probes have been exploited based on various fluorophores such as

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rhodamine, naphthalimide and BODIPY.^{14–16}

Most of the reported pH fluorescent probes have exhibited weak acidic (4-6) or neutral (6-8) response behavior.¹⁷⁻²² However, very few of fluorescent probes have been used for sensitive detection of pH below 4 due to their instability or destructive inactivation under extreme pH condition.^{23–25} Actually the extremely acidic conditions are not suitable for most of the living species, while many microorganisms such as Helicobacter pylori and Acidophiles prefer to live in harsh environments.^{26,27} With the ingestion of food, an acidity pH in the range of 2.0-3.0 is produced by gastric acid in the stomach, then proteins are digested by pepsin converted from pepsinogen.^{28,29} Thus, it is particularly urgent to develop small molecular fluorescent probes to indicate the harsh pH milieu in the fields of biological and environmental science. In comparison with the conventional fluorescent probes, probes derived from natural product can avoid acute cellular rejection and precarious sustained-release property, realize sustainable chemistry and protect the cells from the mostly high-toxic organic fluorophores.^{30,31}







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Longifolene is an important constituent of natural and renewable turpentine and isolongifolanone is directly prepared from longifolene in the presence of oxidants.³² Isolongifolanone can be used to synthesize a variety of valuable derivatives such as α,β unsaturated ketone, pyrazole and pyrimidine, which have been exploited for the applications in the fields of antineoplastic and anophelifuge.³³ Recently, only a few of novel isolongifolanone derivatives have been developed for the biological imaging and chemical sensing applications. A novel hexahydroquinazolin-2amine-based fluorescence sensor for Cu²⁺ was synthesized from isolongifolanone.³⁴ An isolongifolanone-based molecular probe was successfully used for imaging endogenous Zn²⁺ in *vivo.*³⁵ Thus, to design fluorescence probes from isolongifolanone is very meaningful and promising for the exploition of turpentine.

Herein, we reported two novel pH-sensing probes (2–3) synthesized from isolongifolanone. The fluorescence probes 2–3 with D- π -A configuration possess common *N*, *N*-dimethylaniline unit as electron donors, and various electron acceptors involving pyrazole and pyrimidine moieties, respectively. The pH-sensing properties for probes 2–3 were investigated in both solution and solid states. Additionally, the sensing mechanism for H⁺ and potential application in logic gates was proposed.

2. Results and discussion

2.1. Synthesis of compounds 2-3

The synthetic route of compounds **2** and **3** were shown in Scheme **1**. Compound **1** was synthesized by an aldol condensation reaction between isolongifolanone and *p*-dimethylaminobenzaldehyde. Compound **2** was prepared by compound **1** and hydrazine monohydrate *via* a cyclization reaction in the presence of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone as an oxidant. Compound **3** was obtained by a reaction of compound **1** and guanidine hydrochloride using potassium *tert*-butylate as a catalyst in *tert*-butyl alcohol. The desired compounds **2** and **3** were characterized by IR, NMR and HRMS.

2.2. Solvent-dependent properties

The compounds **2**–**3** possessed typical conjugate and aromatic ring structures, in which the strong electron donating dimethyl amino group was attached to pyrazole and pyrimidine matrixes, respectively. The fluorescent properties of compounds **2**–**3** were dependent on the formation of their D- π -A structures in solution, which was greatly affected by the solvent polarity. To further study their photochemical properties, the fluorescent spectra of compounds **2**–**3** (1 × 10⁻⁵ M) were investigated in various solvents such as *n*-hexane (Hex), toluene (Tol), ethyl acetate (EA), trichloromethane (TCM), *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO).

As shown in Fig. 1, the emission spectra of compounds 2-3



Scheme 1. Synthesis of compounds 2–3.



Fig. 1. The solvatochromism of compounds $2-3 (1 \times 10^{-5} \text{ M})$. The fluorescence spectra of compounds (a) $2 (\lambda_{ex} = 325 \text{ nm})$ and (b) $3 (\lambda_{ex} = 300 \text{ nm})$ in different solvents.

showed significant changes with solvent polarity in terms of emission maximum. Compounds 2-3 emitted blue-shifted fluorescence in non-polar solvents, while emitted red-shifted fluorescence in polar solvents. So far, there are many methods to indicate polarity parameter of solvent. However, $E_{T}(30)$ is one of the most consummate approaches among them. $E_T(30)$ is characterized by electron transition energy of UV-vis spectra of Reichardt's Dye due to its specific π - π ^{*} absorption band in ICT progress in different solvents. With the increasing solvent parameters ($E_T(30)$), the emission maximum of compounds 2-3 increased from shorter wavelength ($\lambda_2 = 345 \text{ nm}$ and $\lambda_3 = 380 \text{ nm}$) in *n*-hexane to longer wavelength ($\lambda_2 = 375 \text{ nm}$ and $\lambda_3 = 419 \text{ nm}$) in DMSO. The results show that compounds 2-3 have positive solvatochromism. Moreover, solvent also had a significant effect on the fluorescence quantum yield. As the solvent parameters $(E_T(30))$ increased from *n*-hexane to DMSO, the decrease of quantum yields accompanied with increase of the Stokes shift were presented (Table 1). The direct correlations between solvent polarity parameter ($E_T(30)$) and Stokes shift were plotted for displaying the solvent-dependent fluorescence features of compounds 2-3. Fig. 2 depicted that compounds 2-3 exhibited a linear relationship in Stokes shift interacting with solvent polarity. In addition, compound **3** showed a much larger linear slope than compound **2**, suggesting its larger dipole moment. Because of the increase of the solvent polarity from n-hexane to DMSO, the increased dipole moment leads to a great stabilization and a low energy in excited states of fluorophores, resulting in the red-shifted fluorescence.

2.3. DFT study

To further understand the optical properties of these fluorophores towards H⁺ with density functional theory (DFT), the geometries of compounds 2-3 were optimized using the Gaussian 09 (B3LYP/6-31G(d)).^{36,37} As shown in Fig. 3, the HOMO orbitals of compounds 2-3 with or without H⁺ were distributed over the molecules except for the partial isolongifolanone units, while their LUMO orbitals were primarily located on pyrazole and pyrimidine moiety, respectively, which suggests an obvious ICT (intramolecular charge transfer) effect between the donor part (dimethylamine) and the acceptor parts (pyrazole and pyrimidine), leading to the solvatochromic emission. However, compared with the HOMO and LUMO orbitals of compounds 2-3, the HOMO and LUMO orbitals of compounds 2–3 with H⁺ exhibited more obvious redistributions from the dimethylamine group to the pyrazole and pyrimidine groups. It indicated that the N atoms binding with H⁺ could increase the ICT effect. In addition, the HUMO-LUMO band gaps (ΔE) of compounds 2-3 were found to be 4.86 eV and 4.42 eV, respectively, which correspond to the status of compounds 2-3 as D- π -A fluorophores. Moreover, the ΔE values of compound **2–3** with H⁺ were lower compared with that of free compounds 2-3, indicating its more prominent intramolecular push-pull effect.

Table 1

	Photophysical	data of c	ompounds	2 and 3 i	in various	solvents.
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Solvent	<i>ET</i> (30) (Kcal/mol)	2	2				3			
		$\lambda_{abs} (nm)$	$\lambda_{ems} (nm)$	Stokes shifts (cm ⁻¹)	Φ^{a} (%)	$\lambda_{abs} (nm)$	$\lambda_{ems} (nm)$	Stokes shifts (cm ⁻¹)	Φ^{a} (%)	
Hex	30.9	282	345	6475	70.14	338	380	3270	54.66	
Tol	33.9	283	366	8013	65.24	339	396.5	4278	48.22	
EA	38.1	284	358	7278	54.69	340	404.5	4689	39.23	
TCM	39.1	284	372	8329	10.23	341	414	5171	9.98	
DMF	43.8	285	373.5	8314	24.08	341	418	5402	25.38	
DMSO	45	285	375	8421	23.37	341	419	5459	26.12	

^a The absolute quantum yield (Φ) was directly measured by using an FM-4P-TCSPC transient fluorescence spectrometer and calculated with the formula of $\Phi = [A(em)_s - A(em)_s] \times 100\%$. Where A(em) is the measured integrated fluorescence emission intensity, A(sc) is the integrated Rayleigh scattering intensity, the subscripts s and b refer to compounds (**2**–**3**) and blank (solvent), respectively.



Fig. 2. Dependence of the Stokes shift of compounds 2-3 on polarity parameters (*ET*(30)) of solvents.



Fig. 3. The molecular orbital diagrams of HOMO and LUMO of compounds $\mathbf{2}-\mathbf{3}$ with or without $\mathrm{H}^+.$

2.4. pH sensing

Isolongifolanone-based derivates 2-3 with nitrogenousheterocyclic structures and additional dimethyl amino group afford multiple protonation sites to sense acidic pH change. The pHdependent properties of compounds 2-3 were evaluated through the absorption and fluorescence spectra.

The standard pH titration of absorption spectra and fluorescence spectra of compound **2** were performed in Fig. 4 and Fig. S1. The absorption peak at 285 nm gradually decreased and disappeared with decreasing pH from 7.0 to 1.0, while the absorption peak at 315 nm subsequently appeared and enhanced. Moreover, the fluorescent properties of compound **2** were examined in ethanol-water solutions with different pH values, the corresponding fluorescence spectra are measured. When the pH was decreased from 7.0 to 1.0, compound **2** showed the gradually quenched fluorescence band at 373 nm and the sharply enhanced intensity at 445 nm. Simultaneously, the colour of the solution was changed from dark to bright blue under 365 nm irradiation. The nonlinear pH titration curve was obtained with a pK_a of 2.59 through fluorescence intensity ratio (I_{445}/I_{373}). Furthermore, the fluorescence intensity ratio (I_{445}/I_{373}) of compound **2** afforded a good linearity in the pH range of



Fig. 4. (a) UV–vis absorption spectra of compound **2** (1×10^{-5} M) in EtOH/H₂O (v/ v = 8/2) with decreased pH from 7.0 to 1.0. (b) Absorption intensity changes of compound **2** with pH decrease at 285 nm and 315 nm, respectively. (c) Fluorescence spectra of compound **2** (1×10^{-5} M) in EtOH/H₂O (v/v = 8/2) with decreased pH from 7.0 to 1.0. (d) pH titration curve of compound **2** using the fluorescence emission intensity ratio (I_{445}/I_{373}) (λ_{ex} = 325 nm).

1.5–4.0 with the according equation: I = $-19.110 \times pH+73.872$ (R = 0.9849). The significantly large Stokes shift of compounds **2** under acidic conditions was calculated to be 120 nm, which could help to reduce the excitation interference. The excellent pH-dependent performance indicates compound **2** has a high sensitivity to extreme acid media.

As shown in Fig. 5 and Fig. S2, with the pH decreasing from 7.0 to 1.0, the absorption peak at 342 nm decreased whereas a new band increased at 409 nm. The fluorescence intensity of compound **3** at 434 nm ($\lambda_{ex} = 300$ nm) gradually quenched with the decreasing pH from 7.0 to 1.0, and the nonlinear pH titration curve was plotted with a pK_a of 3.69. Compound **3** also showed a good linear relation response to pH changes in the range of 3.5–7.0 with the according equation: $I = 36.885 \times pH + 142.524$ (R = 0.9887). As the new red-shifted absorption peak at 409 nm evolved below pH = 3.5, we evaluated the pH-responsive properties of compound **3** towards pH over the range of 1.0–3.5 under the longer wavelength of excitation peak ($\lambda_{ex} = 425 \text{ nm}$). In this case, the fluorescence intensity of compound 3 at 519 nm enhanced with the decreased pH from 3.5 to 1.0, and then afforded a good linearity in the pH range of 1.0–3.5 with the according equation: $I = 61.104 \times pH+237.546$ (R = 0.9967). The remarkably large Stokes shift of compounds 3 under acidic conditions was found to be 134 nm. The result shows that compound **3** can be used as a pH sensor for broad acidity.



Fig. 5. (a) UV–vis absorption spectra of compound **3** (1×10^{-5} M) in EtOH/H₂O (v/v = 8/2) with decreased pH from 7.0 to 1.0. (b) Absorption intensity changes of compound **3** with pH decrease at 342 nm and 409 nm, respectively. (c) Fluorescence spectra of compound **3** (1×10^{-5} M) in DMF/H₂O (v/v = 8/2) with decreased pH from 7.0 to 1.0. (d) pH titration curve of compound **3** using the fluorescence emission intensity at 434 nm ($\lambda_{ex} = 300$ nm).

2.5. Sensing mechanism

To understand the pH-sensing mechanism, the ¹H NMR spectra of probes **2–3** before and after the addition of hydrochloric acid (HCl) have been studied in DMSO- d_6 (Fig. 6). When HCl was added into a DMSO- d_6 solution of probe **2**, the hydrogen atom of pyrazole (H-1) was dramatically disappeared. However, the chemical shifts of dimethylaniline-hydrogen showed almost no change (H-2, H-3, H-4, H-5, H-6, H-7), which due to the protonation of N atom in pyrazole moiety rather than dimethylamino group. This result suggested that the preferential protonation of pyrazole N may occur in this process under acidic condition, which resulted in the enhancement of ICT effect from dimethylamino group to pyrazole group. The ¹H NMR signals revealed that probe **3** showed remarkable down-shifts for the hydrogen atoms of 2-amine (H-1) in pyrimidine unit. In contrast, the chemical shifts of the surplus dimethylaniline-hydrogen had almost no change (H-4, H-5, H-6, H-7). This was because of the protonation of N atom in pyrimidine unit rather than dimethylamino group. We can conclude that the N atom of 2-amine in pyrimidine unit was definitely protonated. Meanwhile, the ¹H NMR spectra of probe **3** under acidic pH condition also showed the slight down-shifts for the partial hydrogen atoms of benzene (H-2, H-3) in dimethylaniline moiety, which might be affected by the protonation of pyrimidine ring N atom close to benzene and the para-position substitution (dimethylamino group) on benzene. Upon addition of HCl, the pyrimidine ring N atom close to benzene was first protonated, thus its electron withdrawing ability got stronger, as a result, the another pyrimidine ring N atom away from benzene was no longer protonated because its electron density decreased. In this case, the resulting stronger D- π -A systems led to red-shifted absorption and emission spectra. Therefore, the sensing mechanism of compounds 2-3 for H⁺ was also proposed in Fig. 6.

2.6. Photostability and reversibility

The photostability and response time between compound **2** and H^+ were also evaluated by monitoring the maximum fluorescence intensity in ethanol-water of various pH values (Fig. 7a). The fluorescence intensity of compound **2** could reach saturation within

30 s. Such a rapid response time is crucial for compound **2** to track environmental pH changes in real time. Compound **2** showed the stable fluorescence in the presence of H^+ . As shown in Fig. 7b, the plotted five alternate cycles indicate that compound **2** has excellent reversibility between pH 2.0 and 7.0.

The fluorescence intensity at 434 nm was measured to study the photostability and reversibility of compound **3** for sensing pH in ethanol-water solutions (Fig. 8). The fluorescence intensity of compound **3** remained stable when it was dissolved in solutions with different pH values. Moreover, the reversibility study suggests that compound **3** can provide a reusable environment for detecting the pH values.

2.7. Selectivity studies

The selectivity profile of compounds **2–3** for H⁺ over various metal ions was performed by ultraviolet spectroscopy at pH 7.0 and 1.0. As shown in Fig. 9a, the absorption intensity ratio (A_{315}/A_{285}) of compound **2** at pH 7.0 and 1.0 showed no obvious changes upon addition of various metal ions, such as Cr³⁺, Co²⁺, Ag⁺, Cu²⁺, Hg²⁺, K⁺, La³⁺, Mg²⁺, Na⁺, Pb²⁺, Fe³⁺, Zn²⁺, Al³⁺ and Li⁺. Various metal ions also caused negligible effect on the absorption intensity ratio (A_{409}/A_{342}) of compound **3** at pH 7.0 and 1.0 (Fig. 9b). These results reveal that compounds **2–3** can be used as specific and selective probe for acidic pH with negligible interference from metal ions.

2.8. Application studies

To further study the optical performance of compounds 2-3response to pH change, the fluorescence emission of their solidstate samples before and after grinding with TsOH (p-toluenesulfonic acid) were investigated. Compounds 2 and 3 showed a highly sensitive and rapid response for TsOH in grinding process. The fluorescence color of compound 2 was pale white, but the fluorescence color of compound **2** was blue after evenly grinding with TsOH under 365 nm UV light. However, the blue fluorescence of compound **3** was quenched in the presence of TsOH (Fig. 10a). Next, the fluorescence spectra of corresponding powders were investigated by fluorescent spectroscopy. As shown in Fig. 10b and c, compound **2** with the fluorescence quantum yield of $\Phi = 10.30\%$ showed a more intense red-shifted band at 424 nm (fluorescence quantum yield $\Phi = 22.31\%$) while compound **3** with the fluorescence quantum yield of $\Phi = 21.04\%$ showed an obvious fluorescence quenching (fluorescence quantum yield $\Phi < 1\%$) upon grinding with TsOH. The result indicates that the solid states of compound 2-3are sensitively responsive to the TsOH medium in a short time frame (5 s). Thus, this might be a new and suitable method to monitor the presence of TsOH in solid state.

We also investigated the fluorescence behaviors of the solidstate compounds 2 and 3 to TFA (trifluoroacetic acid) vapor within 5 s. Compounds 2 and 3 were evenly distributed on the nonradiation filter paper when exposed to TFA vapor for 5 s, respectively. As a result, the track with white fluorescence for compound 2 was changed to blue and the track with bright blue fluorescence for compound 3 was changed to green under UV light of 365 nm (Fig. 11a). As shown in Fig. 11b, the fluorescence emission peak of compound 2 was located at 374 nm (fluorescence quantum yield $\Phi = 10.30$) while the red-shifted fluorescence emission peak induced by TFA vapor was located at 423 nm (fluorescence quantum yield $\Phi =$ 31.67%). Similarly, the fluorescence emission band of compound **3** was located at 443 nm (fluorescence quantum yield $\Phi = 10.30\%$) while the red-shifted fluorescence emission band induced by TFA vapor was located at 505 nm (fluorescence quantum yield $\Phi = 12.76\%$) (Fig. 11c). In addition, the CIE chromaticity diagram of compounds 2 and 3 without and with TFA vapor were



Fig. 6. ¹H NMR spectra of probes 2 (up) and 3 (below) in DMSO-d₆ before and after the addition of hydrochloric acid (HCl).



Fig. 7. (a) The change of the fluorescence intensity at 373 nm and 445 nm for compound **2** (1×10^{-5} M) in EtOH/H₂O (v/v = 8/2) with time course at pH 7.0, 5.0, 3.0, 1.0, respectively. (b) The reversible change of the fluorescence intensity at 373 nm and 445 nm for compound **2** (1×10^{-5} M) in EtOH/H₂O (v/v = 8/2) between pH 7.0 and 2.0 ($\lambda_{ex} = 325$ nm).

carried out to show the red-shifted fluorescence (Fig. 11d and e). The values of compound **2** and **3** were calculated to be (0.1607, 0.0616) and (0.1451, 0.1103), whereas the values of their TFA vapor



Fig. 8. (a) The change of the fluorescence intensity at 434 nm for compound **3** $(1 \times 10^{-5} \text{ M})$ in EtOH/H₂O (v/v = 8/2) with time course at pH 7.0, 5.0, 3.0, 7.0, respectively. (b) The reversible change of the fluorescence intensity at 434 nm for compound **3** $(1 \times 10^{-5} \text{ M})$ in EtOH/H₂O (v/v = 8/2) between pH 7.0 and 2.0 ($\lambda_{ex} = 300 \text{ nm}$).

samples were calculated to be (0.1721, 0.1077) and (0.2700, 0.5080), respectively, which were consistent with the solid-state fluores-cence colors displayed on filter paper.



Fig. 9. The ratio of absorption intensity of (a) compound **2** (1×10^{-5} M) at A_{315}/A_{285} ($\lambda_{ex} = 325$ nm) and (b) compound **3** (1×10^{-5} M) at A_{409}/A_{342} ($\lambda_{ex} = 300$ nm) in EtOH/ H₂O (v/v = 8/2) at pH 1.0 and 7.0 in the presence of various metal ions.

To gain further insight into the pH-responsive mechanism of solid-state compounds 2-3, the powder XRD measurements were carried out (Fig. 12). The XRD curves of the pristine fluorophores 2-3 showed many strong and sharp peaks, suggesting their crystalline morphology. However, when compound 2-3 were exposed to TFA, only the weak diffraction peaks were observed. Therefore, the TFA vapor treatment could induce the pronounced collapse of crystalline lattices, which resulted in the significant changes of their solid-state fluorescence emission spectra. Within this context, Compounds 2-3 could recognize TFA vapor with a rapid response time of 5 s, displaying a clear fluorescent response to the surrounding acidic environment in gas phase. Thus, such excellent pH-sensing properties enabled compounds 2-3 to be promising materials in practical applications.

In view of the pH-responsive fluorescence of compound **2**, which showed the one-to-one corresponding emission peaks with the addition of alkali and acid, we construct a novel logic system based on compound **2**. In contrast to many reported molecular logic gates which only perform a single logic operation,^{38,39} the multiple logic systems could be established as a function of the multiple fluorescence signals stimulated by surrounding pH changes. In these logic frameworks, the aqueous solution of compound **2** was used as a gate, while alkali and acid were served as chemical inputs and fluorescence signals as optical outputs (Fig. 13). Moreover, on the basis of the excellent pH reversibility, the multiple-framework logic gate was rationally designed. The binary 1 and 0 were defined in the presence and absence of chemical inputs, respectively. With the distribution of the chemical inputs, the fluorescence signals at 445 nm and 373 nm were served as two outputs in the INHIBIT



Fig. 11. (a) Images of compounds **2–3** before and after fuming with TFA vapor for 5 s. (b) The change of fluorescence spectra of compound **2** upon fuming with TFA vapor ($\lambda_{ex} = 325$ nm). (c) The change of fluorescence spectra of compound **3** upon fuming with TFA vapor ($\lambda_{ex} = 300$ nm). The CIE chromaticity coordinates of compounds (d) **2** and (e) **3** upon fuming with TFA vapor.







Fig. 10. (a) Fluorescence Images of compounds **2**–**3** before and after grinding with 30 equivalents TsOH for 10 s. (b) The change of fluorescence spectra of compounds **2** upon grinding with TsOH ($\lambda_{ex} = 325$ nm). (c) The change of fluorescence spectra of compounds **3** upon grinding with TsOH ($\lambda_{ex} = 300$ nm).



Fig. 13. Logic scheme and truth table of the INH and IMP logic gates of compound 2.

(INH) logic gate and IMPLICATION (IMP) logic gate, respectively. The exploition of dual-output INH/IMP logic gate based on the sensitive and reversible pH response of compound **2** could provide an important addition to potential applications in optical devices.

3. Conclusion

Two novel pH-sensing probes **2–3** were designed and synthesized from renewable isolongifolanone. All of these probes showed positive solvatochromism because of their typical conjugated D- π -A configurations, which was further confirmed by DFT calculations. More importantly, the probes **2–3** with different electron acceptors exhibited differentiated fluorescence emission changes along with decreased pH values due to their varying ICT processes. The excellent pH-responsive performance in solution (HCl) and in the solid (TsOH) and in the gas (TFA) may enable these probes to become the practical reagents for monitoring pH changes in various system. Based on the sensitive and reversible pH response, a multiple-framework logic gate for the probe **2** was also successfully constructed. Our work may pave a way to exploite the utilization of turpentine and provide a possible route for deep processing of forest resources.

4. Experimental section

4.1. Instruments

¹³C NMR and ¹H NMR spectra were recorded in CDCl₃ and DMSO-*d*₆ solutions on Bruker AV 400MZ/600MZ spectrometer. Fluorescence spectra were recorded on Perkin Elmer LS 55 fluorescence spectrophotometer. Mass spectra and infrared spectra were recorded on America Agilent 5975c mass spectrometer and Nicolet 380 FTIR infrared spectrometer, respectively. The purity and melting points were measured on America Agilent 7890A gas chromatograph and X-6 microscopic melting point apparatus, respectively. The fluorescence quantum yield (Φ) was measured by an FM-4P-TCSPC transient fluorescence spectrometer. The pH values were given on a Model PHS-3C pH meter.

4.2. Materials

All the organic solvents and reagents were purchased from commercial sources and used without further purification. Deionized water and analytical grade solvents were used throughout the experiment. The ethanol-water solutions of different pH were prepared using HCl and NaOH solutions at the concentration of 1 M for pH slight adjustment. The salts used in the stock solutions of various metal ions were AgNO₃, Fe(NO₃)₃·9H₂O, CuCl₂·H₂O, FeCl₂, KCl, ZnCl₂, NaCl, Co(NO₃)₂·6H₂O, HgSO₄, La(NO₃)₃·6H₂O, CaCl₂, CrCl₃·6H₂O, MgSO₄, Pb(NO₃)₂, Al(NO₃)₃·9H₂O, respectively.

4.3. Synthesis of 7-(4'-(dimethylamino)benzylidene)isolongifolanone (1)

Isolongifolanone (8 mmol), tert-butyl alcohol (30 ml), potassium *tert*-butoxide (5 mmol) and *p*-dimethylaminobenzaldehyde (10 mmol) were successively added into a 50 ml dried three-necked flask equipped with a stirrer, condenser and thermometer. The mixture was stirred and refluxed for 2 h until the conversion ratio of isolongifolanone exceeded 95% (monitored by GC). The reacted solution was evaporated under vacuum and extracted three times with 20 ml ethyl acetate, the merged organic layers were then washed to neutrality with saturated salt water, dried with sodium sulfate, filtered, evaporated to afford a crude product, and then recrystallized to obtain the compound 1 with ethanol in a refrigerator. The final product was a brown crystal, (90.4%, yield); m.p. 119.5–120.2 °C; FT-IR (KBr, cm⁻¹) v: 2960, 2923, 2891, 2872, 1656, 1606, 1565, 1522, 1466, 1440, 822; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 0.77 (s, 6H), 1.03 (s, 3H), 1.06-1.09 (m, 1H), 1.15 (s, 3H), 1.23 (d, J = 8 Hz, 1H), 1.42–1.49 (m, 1H), 1.55–1.61 (m, 1H), 1.69–1.70 (m, 1H), 1.73-1.75 (m, 2H), 1.81 (s, 1H), 2.53-2.57 (m, 1H), 2.82 (d, J = 16 Hz, 1H), 2.96 (s, 6H, Ar-N(CH₃)₂), 6.74 (d, J = 8 Hz, 2H), 7.34–7.45 (m, 3H); ¹³C NMR (100 MHz, DMSO- d_6) δ : 24.08, 24.47, 25.46, 25.63, 28.40, 29.92, 31.40, 37.28, 39.82, 41.76, 44.20, 47.65, 55.11, 62.28, 111.87, 122.91, 130.17, 132.68, 136.75, 150.64, 200.47; EIMS *m*/*z* (%): 351 (M⁺, 100), 336 (5), 282 (10), 269 (22), 240 (4), 158 (28), 134 (28), 121 (11), 91 (9), 55 (10). Anal. calcd for C₂₄H₃₃NO: C 82.00, H 9.46, N 3.98; found C 82.17, H 9.52, N 3.96.

4.4. Synthesis of 5,5,9,9-tetramethyl-3-(4'-(dimethylamino) phenyl)-2,4,5,6,7,8,9,9a-octahydro-8H-5a,8 methano-indazole (2)

7-(4'-(dimethylamino)benzylidene)-isolongifolanone 1 (8 mmol), hydrazine hydrate (48 mmol), and ethanol (50 ml) were successively added into a 100 ml dried three-necked flask equipped with a stirrer, condenser and thermometer. The mixture was stirred and refluxed for 10 h until the conversion ratio of 7-(4'-(dimethylamino)benzylidene)-isolongifolanone was over 95% (monitored by GC). The reacted mixture was evaporated under vacuum and added with 1,4-dioxane (40 ml) and 2,3-Dichloro-5,6-dicyano-1,4benzoquinone (DDQ, 8.5 mmol) to continuous refluxed reaction for 8 h. After adding 20 ml potassium hydroxide solution and 50 ml dichloromethane, the reacted solution was stirred for 30 min at room temperature, then it was extracted three times with dichloromethane, and the combined organic layers were then washed to neutrality with saturated brines, dried with sodium sulfate, filtered, evaporated to afford a viscous liquid, purified by silica gel column chromatography, and then recrystallized to obtain the compound **2** with ethanol in a refrigerator. The final product was a brown crystal, (73.1%, yield); m.p. 198.3-199.1 °C; FT-IR (KBr, cm⁻¹) *v*: 3233, 2962, 2872, 1616, 1538, 1462, 1439, 1357, 815 cm⁻¹; ¹H NMR (400 MHz, DMSO- d_6) δ : 0.65 (s, 3H), 0.76 (s, 3H), 1.04 (s, 3H), 1.11–1.17 (m, 1H), 1.19 (d, J = 9.7 Hz, 1H), 1.24 (s, 3H), 1.42–1.49 (m, 1H), 1.58 (d, J = 9.5 Hz, 1H), 1.66–1.71 (m, 2H), 1.80–1.84 (m, 1H), 2.21 (s, 1H), 2.28 (d, *J* = 15.1 Hz, 1H), 2.59 (d, *J* = 15.0 Hz, 1H), 2.91 (s, 6H, N(CH₃)₂), 6.76 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.3 Hz, 2H), 12.22 (brs, 1H, NH); 13 C NMR (100 MHz, CDCl₃) δ : 23.51, 25.37, 26.06, 27.15, 28.30, 28.37, 29.70, 34.09, 35.95, 36.74, 40.50, 42.17, 48.33, 51.06, 56.43, 110.98, 112.45, 127.61, 149.79; EIMS m/z (%): 363(M⁺, 100), 348(6), 281(15); HRMS (m/z): [M+H]⁺ calcd for C₂₄H₃₃N₃: 364.2746, found: 364.2723.

4.5. Synthesis of 4-(4'-(dimethylamino)phenyl)-6,6,10,10tetramethyl-5,7,8,9,10,10a-hexahydro-6H-6a,9-methanobenzo[h] quinazolin-2-amine (**3**)

7-(4'-(dimethylamino)benzylidene)-isolongifolanone (5 mmol), guanidine hydrochloride (20 mmol), tert-butyl alcohol (60 ml) and tert-butoxide (25 mmol) were successively added into a 100 ml dried three-necked flask equipped with a stirrer, condenser and thermometer. The mixture was stirred and refluxed for 18 h until the conversion ratio of 7-arylidene-isolongifolanone was over 95% (monitored by GC). The reacted mixture was evaporated under vacuum and extracted three times with ethyl acetate, and the combined organic layers were then washed to neutrality with saturated brines, dried with sodium sulfate, filtered, evaporated to afford a viscous liquid, and then recrystallized to obtain the compound **3** with ethanol in a refrigerator. The final product was a transparent crystal, (84.2%, yield); m.p. 211.3–211.9 °C; FT-IR (KBr, cm⁻¹) *v*: 3487, 3274, 3147, 2957, 2872, 1608, 1547, 1453, 1364, 1195, 944, 819; ¹H NMR (400 MHz, DMSO-*d*₆) δ: 0.55 (s, 3H), 0.74 (s, 3H), 0.94 (s, 3H), 1.05–1.09 (m, 1H), 1.16 (t, J = 8 Hz, 1H), 1.30 (s, 3H), 1.44–1.50 (m, 1H), 1.56–1.63 (m, 1H), 1.69 (d, J=4 Hz, 1H), 1.76–1.88 (m, 2H), 2.13 (d, J = 16 Hz, 2H), 2.81 (d, J = 16 Hz, 1H), 2.95 (s, 6H, N(CH₃)₂), 5.96 (s, 2H, NH₂), 6.73 (d, *I* = 8 Hz, 2H), 7.46 (d, I = 8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ ; 22.79, 24.43, 25.36, 25.53, 26.28, 28.15, 29.74, 32.27, 36.78, 39.84, 43.65, 47.41, 54.71, 57.34, 110.94, 113.35, 125.82, 130.22, 150.46, 160.80, 164.98, 167.74; EIMS *m*/*z* (%): 390 (M⁺, 100), 375 (19), 361 (23), 347 (12), 321 (20), 309 (18), 308 (73), 307 (24), 293 (12), 267 (13), 147 (12), 77 (4), 55 (7); HRMS (m/z): $[M+H]^+$ calcd for C₂₅H₃₄N₄: 391.2855, found: 391.2865.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.tet.2018.05.008.

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