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Tunable phenothiazine hydrazones as colour displaying, ratiometric and reversible pH sensors

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Design, synthesis and characterization of pH responsive, ratiometric and colorimetric phenothiazine hydrazone sensors have been described. Structural modifications in probes **1**–**3** lead to fine tuning of colour, absorption and pH in both acidic and basic pH ranges. Probe **1** acts as a pH sensor in 11–14 pH range with a tetracolour change from yellow to orange to red to magenta-purple whereas **3** acts as a pH sensor in 2–9 pH range accompanied by a colour change from pale-yellow to yellow. Probe **3** also displays fluorescence quenching through d-PET mechanism. NMR studies were performed to get an insight into the interaction of the probes (**1**–**3**) with H^+/OH^-. UV absorption, fluorescence emission and colour switching of the synthesized molecules were found to be reversible upon a change in the pH.

Introduction

Molecules having pH-responsive optical properties have gained increasing popularity in the investigation of biological processes,[1] medicine,[2] cellular imaging,[3] environmental studies,[4] extent of corrosion of steel reinforced concrete structures,[5] etc. by monitoring the variation in pH. Many electrochemical pH sensors are reported in the literature.[6] However, optical sensors offer several advantages including naked eye detection and design modulation, etc.[7] Thus, design and development of colorimetric chemosensors for prompt recognition of pH changes by naked eye detection is important.

Aromatic hydrazones have displayed anticancer,[8] antifungal,[9] anti-inflammatory,[10] antimicrobial,[11] and anti-HIV[12] activities. They have also shown promising material properties in the field of electrophotographic photoreceptors, optoelectronic devices,[13] and sensors.[7e,14] Phenothiazine-based hydrazones have attracted considerable attention because of their diverse applications as hole-transporting materials,[15] photoconductive glass-forming materials,[16] etc. As part of our research work on the synthesis of probes for single analytes,[17] we have designed novel phenothiazine hydrazones (**1** and **2**) (Fig. 1). We considered that, phenothiazine is an efficient chromophore and an excellent electron donor (D), thus its combination with pH responsive hydrazone moiety in a single framework may lead to interesting pH responsive chromogenic material. Also, the other end of the hydrazone moiety is appended with phenyl ring end-capped with electron-withdrawing NO_2 or CN as acceptor (A) to make imino hydrogen more acidic. Thus, we envisaged that these novel molecules (**1** and **2**) with pH-responsive hydrazone group, may act as pH sensors upon deprotonation in basic media.

In order to tune the sensing ability of hydrazones towards acidic pH, probe **3** was designed (Fig. 2). It consists of typical 'fluorophore-spacer-receptor' d-PET design, that is, the fluorophore acts as the electron donor of the PET process. Probes containing electron-donating fluorophores like carbazoles, phenothiazines, etc. are known to exhibit reverse PET or d-PET effect.[18] We reasoned that in acidic medium, phenothiazine fluorophore being a strong electron donor will transfer electron to the protonated pyridine ring (receptor) by d-PET mechanism. Thus, we expected **3** to exhibit quenching of fluorescence by d-PET effect in acidic medium. Herein, we describe synthesis and application of novel phenothiazine hydrazones (**1**–**3**) as pH sensors. Probe **1** proved to be good sensor in 11–14 pH range whereas probe **3** based on d-PET design acted as a pH sensor between a range of 2 and 9.

Results and discussion

Synthesis of probes (1–3)

Phenothiazine-based hydrazones (**1**–**3**) were synthesized in excellent yields (80–98%) by the condensation reaction of 10-ethyl-10*H*-phenothiazine-3-carbaldehyde with arylhydrazines

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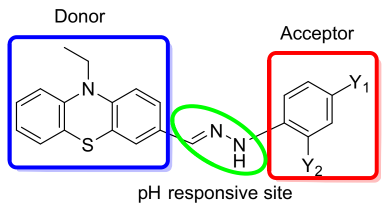
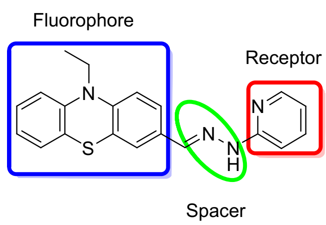


1; Y_1 and Y_2 = NO_2
2; Y_1 = CN and Y_2 = H

Figure 1. Design of phenothiazine hydrazones **1** and **2**.



3

Figure 2. Design of phenothiazine hydrazone **3**.

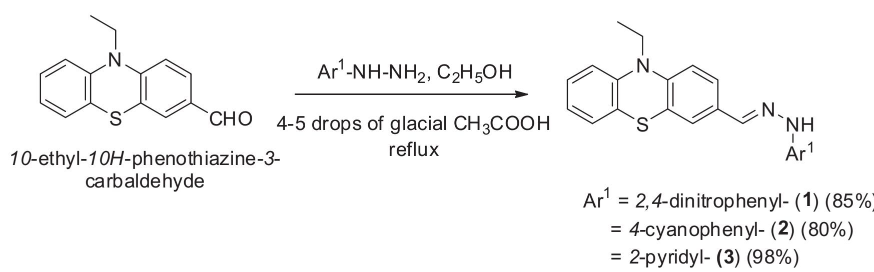
in the presence of a few drops of glacial acetic acid as shown in scheme 1. The ^{1}H NMR spectra of **1–3** displayed a peak at δ 11.54, 10.86 and 10.74, respectively, due to NH proton, thus confirming the formation of hydrazones. The chemical structures of synthesized probes were further confirmed by ^{13}C NMR, IR and HRMS spectral data.

The molecular structure of **2** was also confirmed by single crystal X-ray diffraction studies (CCDC 1412793).[19] Crystals of **2** were grown in chloroform/petroleum ether mixture (Fig. 3i). The synthesized bipolar molecule **2** adopts an 'E' configuration with phenothiazine moiety and 4-cyanophenyl ring being located on the opposite sides of C=N bond. The crystal structure exhibited antiparallel face to face π–π stacking between electron-rich phenothiazine ring and electron-deficient 4-cyano-phenyl ring of two molecules with interfacial centroid distance of 4.059 Å (Fig. 3ii).

Colorimetric studies

DMSO solutions of Probes **1** (5×10^{-5} mol L^{-1}) and **3** (5×10^{-5} mol L^{-1}) displayed instantaneous and reversible colour change on changing pH. The solution of **1** changed colour from yellow to orange to red to magenta-purple in the pH range of 10.5–14 (Fig. 4) whereas a solution of **3** which was initially pale yellow changed to yellow in the pH range of 10–2 (Fig. 5). No noticeable colour change was observed in the case of DMSO solution of **2** (5×10^{-5} mol L^{-1}).

UV–Vis studies. In order to investigate the pH sensing behaviour of probes, UV–vis spectrophotometric titrations of **1–3** (5×10^{-5} mol L^{-1}) were conducted in DMSO. DMSO solution of **1** showed λ_{max} at 442 nm at pH 10.5 (Fig. 6i) whereas two maxima were displayed in the absorption spectrum of **2** (341 and 394 nm) at pH 11 (Fig. S1) and **3** (322 and 375 nm) at pH 10.2 (Fig. 7i). When



Scheme 1. Synthetic route to phenothiazine-based hydrazones (**1–3**).

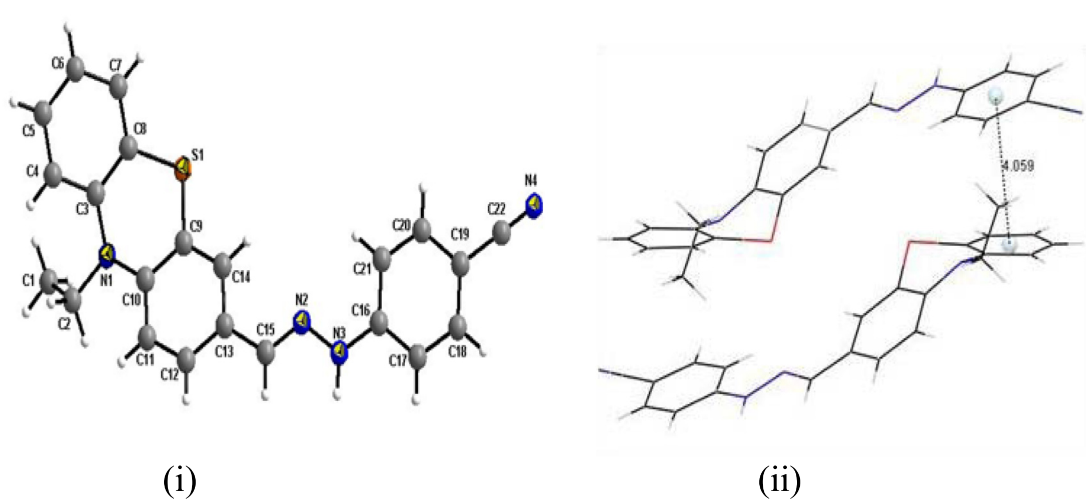


Figure 3. (i) Molecular structure of **2** (CCDC 1412793) at 50% probability level. (ii) Antiparallel face to face π–π interaction between adjacent molecules of **2** (when viewed along *b* axis).

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