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A novel PBT-based fluorescent probe for hydrazine detection and its application in living cells

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ABSTRACT

A new 2-phenyl-benzothiazole (PBT) based fluorescent probe (AcO-PBT-CHO) was designed and synthesized for the detection of hydrazine. The aldehyde and acetyl ester groups were used as the recognition units. Upon the treatment of the probe with hydrazine, the emission at 505 nm decreased while the emission at 430 nm increased. Accordingly, the fluorescent color changed from green to blue. The aldehyde and acetyl ester groups exerted additive effect on the fluorescence spectrum changes of the probe. The probe could selectively identify hydrazine over other related interfering species. The probe could detect hydrazine quantitatively in the range of 20–40 μM with the detection limit of 2.80 ppb. Furthermore, the probe was successfully applied to detect hydrazine in living cells.

1. Introduction

Hydrazine is a strong reducing agent and highly reactive base. It plays an important role in the chemical, pharmaceutical and agricultural industries involving catalysts, photography chemicals, pesticides, various dyes, pharmaceutical intermediates and so on [1,2]. Meanwhile it is famous as a high-energy fuel in rocket propulsion systems due to its flammable and detonable characteristics [3]. In industry, it is often used as a chemical blowing agent and corrosion inhibitor for heating system [4]. However, hydrazine is extremely toxic and easily absorbed by oral, dermal, and inhalation exposure routes. Animal experiments suggested that hydrazine is highly mutagenic and carcinogenic [5]. Hydrazine is also a neurotoxin and has severe mutagenic effects causing severe damage to the liver, lungs, kidneys and human central nervous system [6]. Therefore, the design and synthesis of sensitive and selective hydrazine probes have attracted much attention in recent years.

Varieties of methods for hydrazine detection have been developed, including spectroscopy, liquid/gas chromatography, electrochemistry, titrimetry and so on [7–11]. However, these conventional methods have several common defects such as time-consuming, low sensitivity and sophisticated process, which limits the practical application in hydrazine detection. In contrast, fluorescence based techniques have the characteristics of high sensitivity, distinctive selectivity and easy operation. Fluorescent probes have recently drawn the attention from the analytical community [12–16]. Among many sophisticated optical signaling systems, reactive chemical probes have received much interest due to their specificity and cumulative signaling effects [17–21]. There are numerous elaborately designed reactive probe systems for the analysis of metal ions, anions, and neutral molecules utilizing unique chemical transformations [22–25]. Our research group has been involved in the synthesis of various chemosensors for the selective recognition of ions and molecules [26,27]. As for the hydrazine detection, there are many recognition sites applied on reactive fluorescent probes, including acetate [28–31], aldehyde [32,33], dicyanovinyl [34–37], phthalimide [38,39], 4-bromobutanoate [40,41], 4-oxopentanoate [42,43], etc [44–46]. Nevertheless, these current reports still suffer from strong background signals, poor selectivity, high detection limit and narrow measurement range. Hence, it remains a significant challenge to develop new strategies to monitor hydrazine. Up to now, few fluorescent chemodosimeters with two different reaction sites for hydrazine have been reported [47]. In this work, we selected acetate and aldehyde as two distinct reaction units for hydrazine recognition, which showed good sensitivity and selectivity toward hydrazine. The probe could be also applied in the imaging of hydrazine in living cells.

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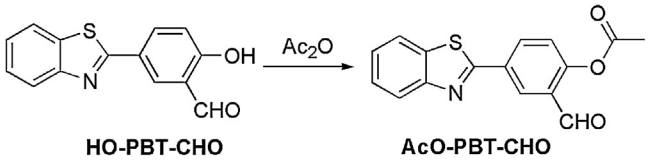
2. Materials and instrumental methods

2.1. Experimental section

All reagents and solvents were analytical grade without further purification. 4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) was purchased from Sigma-Aldrich (St. Louis, MO). HO-PBT-CHO was synthesized according to the literature method [48]. PBT-CHO was synthesized according to the literature method [49]. H_2O was deionized. The solutions of anions and cations were prepared from their sodium salts and chloride salts, respectively. ^1H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were recorded on Bruker AVANCE III spectrometer with tetramethylsilane (TMS) as the internal standard. HRMS were obtained on Fourier transform ion cyclotron resonance mass spectrometry (Bruker, Apex Ultra 7.0T). Fluorescence measurements were carried out on an Agilent Cary Eclipse fluorescence spectrophotometer. Infrared spectrum were obtained on a Thermo Nicolet iS10 spectrometer. A ZEISS LSM 880 confocal fluorescence microscope was used in the vivo experiment.

2.2. Synthesis of the probe

HO-PBT-CHO (510 mg, 2 mmol) was dissolved in acetic anhydride (3.0 ml, 30 mmol). The resulting mixture was stirred at reflux for 3 h. Water (5.0 ml) was added to the reaction mixture. Solid was precipitated from the solution, which was collected by filtration and washed several times with water to give the desired product as a white solid (368 mg, 62%) (Scheme 1). ^1H NMR (600 MHz, DMSO-d_6): δ 2.40 (s, 3H), 7.50-7.56 (m, 2H), 7.59 (t, J = 12 Hz, 1H), 8.13 (d, J = 12 Hz, 1H), 8.21 (d, J = 6 Hz, 1H), 8.44 (dd, J = 6, 12 Hz, 1H), 8.60 (d, J = 6 Hz, 1H), 10.20 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 189.76, 169.00, 165.25, 153.42, 152.74, 134.70, 133.70, 131.12, 129.29, 128.51, 126.88 125.88, 125.16, 123.07, 122.52, 20.84. HRMS (ESI, m/z): $[M+H]^+$ calcd for $C_{16}H_{12}NO_3S$: 298.3284; found:. 298.0531.



Scheme 1. Synthesis of the probe.

2.3. General fluorescence spectra measurements

Stock solutions of the probe (10 μM) was prepared in CH_3OH-HEPES (1/1, v/v, PH = 7.4, 10 mM HEPES) solution. Stock solutions (2 mM) of various analytes were prepared in deionized water. The original volume of the receptor solution was 2 ml. And any changes in the fluorescence intensity were monitored using a fluorescence spectrometer (E_x = 360 nm, slit: 5 nm/5 nm).

2.4. Cell culture and fluorescence imaging

BT-474 breast cancer cells (ATCC® HTB-20, over expression of HER2) was cultured at 37 °C in a 5% CO_2 atmosphere and grown in Gibco® RPMI 1640 medium supplemented with 10% fetal bovine serum (FBS) and 0.1% antibotic-antimycotic mix antibiotic

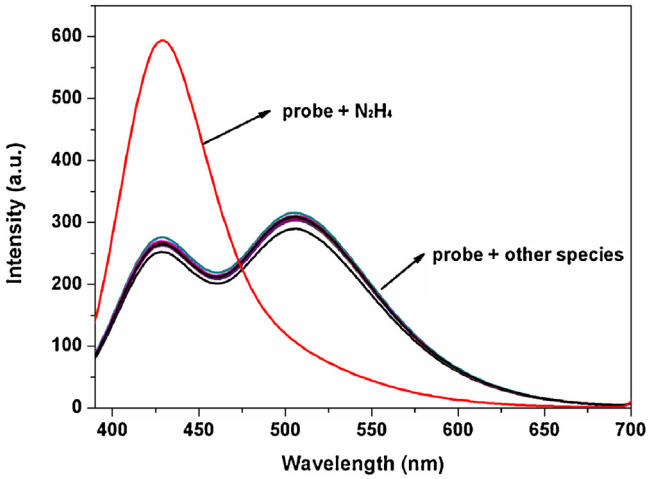


Fig. 2. Fluorescence spectra of the probe (10 μM) in the presence of hydrazine (25 equiv) and other representative metal ions including Mg^{2+}, Ca^{2+}, Hg^{2+}, Au^{3+}, Ba^{2+}, Na^+, K^+, respectively; anions and neutral analytes including Br^-, I^-, F^-, OAC^-, NO_3^-, ClO_4^-, SCN^-, NO_2^-, Ala, Pro, Gly, Ile, urea respectively (250 equiv each) in CH_3OH-HEPES (1/1, v/v, PH = 7.4, 10 mM HEPES) solution at room temperature (λ_{ex} = 360 nm, Each spectrum was recorded after 20 min of mixing).

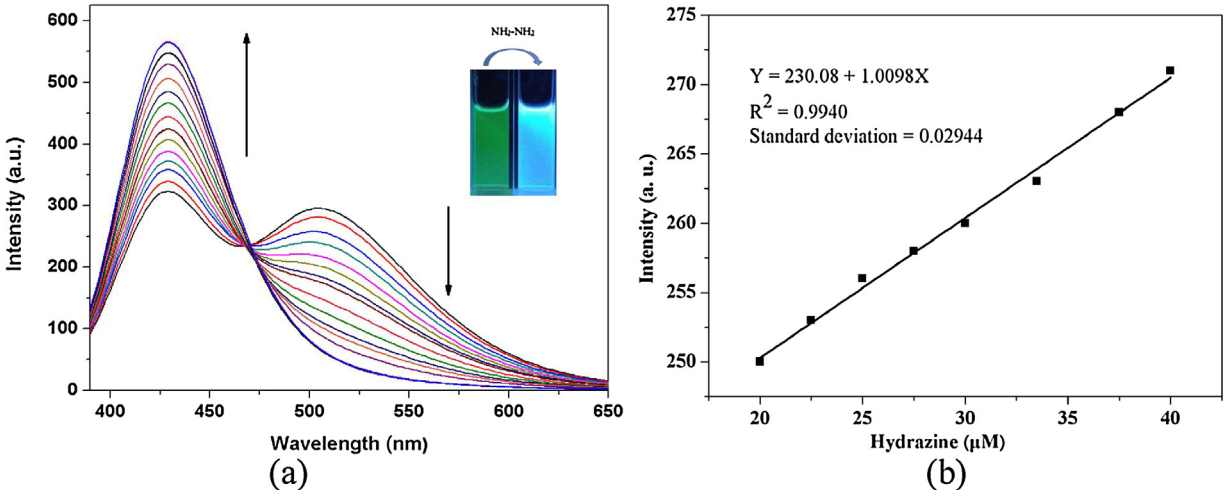


Fig. 1. (a) Fluorescence spectra of the probe (10 μM) upon the addition of increasing amount of N_2H_4 (up to 25 equiv.) in $CH_3OH—H_2O$ (1/1, v/v, PH = 7.4, 10 mM HEPES bufer) solution at room temperature (λ_{ex} = 360 nm). Spectra were recorded after 60 s of each mixing. (b) Fluorescence responses of the probe (10 μM) at 430 nm toward different concentrations of N_2H_4.