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Turn-on fluorescent detection of strong acids based on a naphthalimide-indoline hybrid

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ABSTRACT

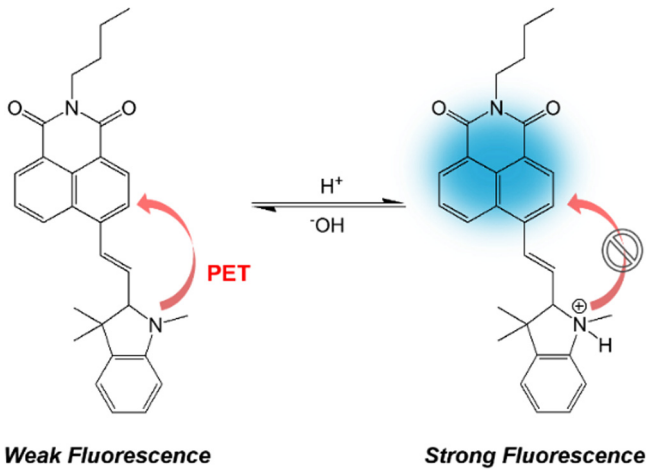
A naphthalimide-indoline hybrid (**1**) was developed as a pH-sensitive turn-on fluorescent probe. Probe **1** displays a weak fluorescence intensity in pH span of 2.5–11.0 owing to a photo-induced electron transfer (PET) from the indoline moiety to the naphthalimide. However, the PET process is suppressed under the pH of 2.5, showing a strong fluorescence signal at 430 nm. The turn-on fluorescent change of **1** is selective for the acidity (H^+) over other anions, metal ions, redox species and it displays a good reversibility. Moreover, glass TLC plates coated with probe **1** can readily detect acid vapors at an ambient atmosphere.

Introduction

Measuring pH is very important in biology, industry, and environments.[1,2] In biology, pH regulates the activity of enzymes involved in a variety of biological processes. For example, mammalian cells have some organelles such as mitochondria, lysosome, endoplasmic reticulum, etc.,[3] and their pH ranges from 4 to 8 depending on the biological functions in the cell. In addition, the pH of gastric acid ranges from 1.5 to 3.5 in the human stomach and it plays a crucial role in digestion by activating digestive enzymes.[4] The inappropriate pH has been associated with various human diseases.[5] However, in the industry, strong acids such as HCl, HF, and etc., are widely used for glass etching, metal cleaning, and electronic manufacturing. Exposure to the acids can cause severe chemical burns and fatal systemic toxicity.[6,7] Thus, acid liquids and vapors must be strictly regulated in manufacturing environments and their leak should be monitored rapidly. Therefore, an effective and rapid detection of pH is extremely important to human being.

So far, glass electrodes are commonly used in pH measurement. But, this method has limitations in analysis environments because it is subject to chemical attack by strong acids, concentrated alkaline solutions, diluted HF, and etc.[8,9] In addition, the glass electrode can be easily broken and thus it should be handled with care. Currently, a number of fluorescent probes are exploited for pH measurement.[10–12] The probes provide changes in the fluorescence signal to pH with a high sensitivity, and a rapid response time. But their working range is usually pH 4–11 and only a few fluorescent sensors are available for the detection of the extremely acidic pH region.[13,14]

In this study, we presented a naphthalimide-indoline hybrid (**1**) as an acidic pH-sensitive turn-on fluorescent probe. As illustrated in Scheme 1, probe **1** shows a weak fluorescence in neutral and



Scheme 1. Proposed pH-dependent fluorescent turn-on mechanism of probe **1**.

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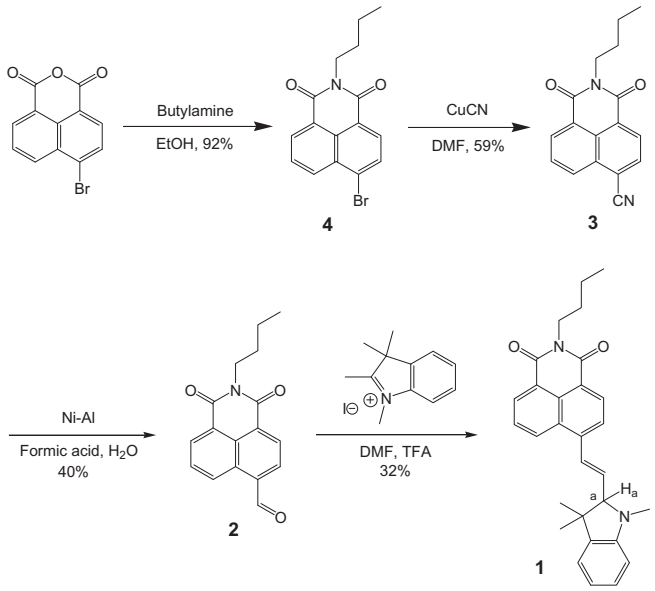

Scheme 2. Synthetic routes to a naphthalimide-indoline hybrid (**1**).

basic solutions, presumably due to a photo-induced electron transfer (PET) that might occur from the nitrogen atom of indoline moiety to the naphthalimide part. However, in case of the acidic solution, a protonation of the indoline induces a suppression of the PET process, which gives rise to a fluorescence increase. Thus, probe **1** provides a fluorescence change in a turn-on manner towards pH variations. Photophysical changes of **1** to pH variations and its sensing mechanism was investigated using absorption and fluorescence spectroscopy, as well as ^{1}H NMR spectroscopic studies.

Results and discussion

Reagents and materials

All reagents, including perchlorate (ClO_4^-) salts of metal ions, tetrabutylammonium (TBA) salts of anions, thiols such as glutathione (GSH), cysteine (Cys), homocysteine (Hcy), sodium hydrosulfide for SH_2 generation and other chemicals for synthesis and analysis were purchased from Aldrich, TCI, Alfa and used as received. All solvents were HPLC reagent grade, and distilled water was used in the analytical experiments. NMR was recorded at Varian 400 MHz and Bruker 500 MHz instrument and all chemical shifts are reported in ppm value using TMS as an internal reference. ESI-MS data were obtained using liquid chromatography mass spectrometer (LC/MS) at the Korea Basic Science Institute.

UV/Vis absorption and fluorescence spectroscopy

Stock solutions of probes, perchlorate salts of metal ions, and TBA salts of anions were prepared in CH_3CN. The pH buffer solutions were prepared by using 50 mM of potassium chloride (for pH 1–2 buffer), potassium hydrogen phthalate (for pH 3–5 buffer), potassium dihydrogen phosphate (for pH 6–8 buffer), sodium tetraborate (for pH 9–10 buffer), and sodium bicarbonate (for pH 11 buffer). The pH was adjusted by adding 0.1 M of NaOH or 0.1 M of HCl solutions. Stock solutions of reactive oxygen species were prepared by using literature procedures.[15] Briefly, H_2O_2, *tert*-butylhydroperoxide (HOO^{t}Bu), and hypochlorite (NaOCl) were delivered from 35%, 70%, and 11–14% aqueous solutions respectively. Hydroxyl radical (HO$^\cdot$) and *tert*-butoxy radical (^{t}BuO$^\cdot$) were generated by the reaction of 10 mM $(NH_4)_2Fe(SO_4)_2$, with 10 mM H_2O_2 or HOO^{t}Bu, respectively. Superoxide (O_2^-) was delivered from 10 mM of potassium oxide (KO_2) in 10 mM pH 7.4 PBS solution. The Cu^+ was delivered from $[Cu(MeCN)_4][PF_6]$ in CH_3CN solution.[16]

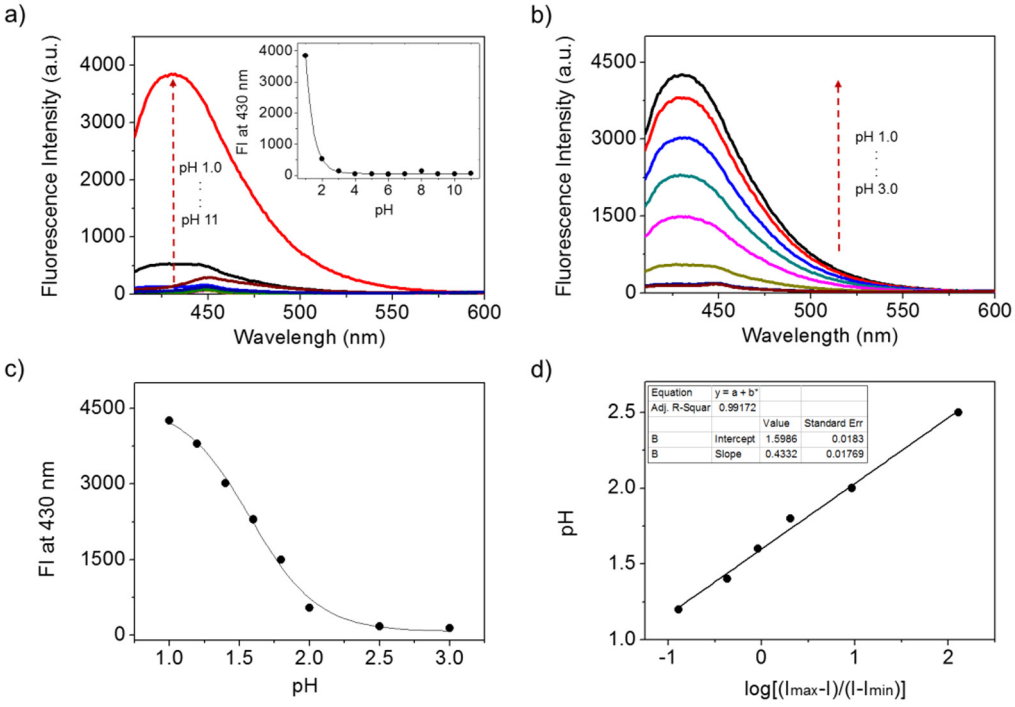

Fig. 1. Fluorescence response of **1** to pH variations. (a) Fluorescence spectra of **1** (10.0 μM) at different pH values (1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, 10, 11). Inset: plot of fluorescence intensity (FI) at 430 nm *vs* pH. (b) Fluorescence spectra of **1** (10.0 μM) recorded at pH span of 1–3 (1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.5, 3.0). (c) Plot of FI at 430 nm *vs* pH obtained from (b). (d) Plot of pH *vs* $\log[(I_{max} - I)/(I - I_{min})]$, where I is the observed fluorescence intensity of **1** at 430 nm. The y-intercept is the pK_a value (1.60 ± 0.018) of **1**. All data were obtained using an excitation at 390 nm in 50.0 mM buffer solution containing 10% (v/v) CH_3CN at room temperature.