Talanta 189 (2018) 39–44

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Benzothiazole modified rhodol as chemodosimeter for the detection of sulfur mustard simulant

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ARTICLE INFO

Keywords:
Rhodol
Sensors
Excited state intramolecular proton transfer
Mustard
Spiro compounds

ABSTRACT

In this paper, we introduced a new sensor for detecting sulfur mustard (**SM**) and its simulant through the functionalization of a rhodol chromophore with benzothiazole, followed by thionation of the spirolactam. The synthesized chemodosimeter (**RHBT**) exhibited an obvious green-yellow fluorescence enhancement and chromogenic change from colorless to fuchsia in the presence of **SM** and its simulant stimuli, which is based on the spirothiolactam ring opening of rhodol induced by the synergy of *S*-alkylation of thiolactam and the excited state intramolecular proton transfer (**ESIPT**) of rhodol–benzothiazole. Furthermore, the chemodosimeter was successfully demonstrated for the rapid detection of **SM** and its simulant in solution, soil and air at ambient temperature, indicating its potential application for on-site detection of sulfur mustard.

1. Introduction

Sulfur mustard (**SM**, or mustard gas) is a severe erosive agent that can cause grievous blisters on the skin and mucous membranes [1]. **SM** is also an alkylating agent that can react with guanine nucleotides in DNA, resulting in mutagenic, carcinogenic and teratogenic effects with long-term exposure [2]. In recent years, there have been many poisoning incidents induced by mustard gas which was left over during World War II [3]. Besides the large amounts of stockpiled (or hidden) mustard gas, it is increasingly considered a terrorist threat to humankind and homeland security due to its easy preparation and low cost [4]. Therefore, developing a simple and effective detection strategy for on-site detection of trace amounts of mustard gas is highly desirable and significant.

At present, the usual methods to detect mustard gas include infrared spectroscopy, liquid chromatography, gas chromatography (GC), gas chromatography-mass spectrometry (GC-MS), and GC-MS combined with some other enrichment technologies [5]. These traditional detection methods have their own advantages, but the drawbacks are also extremely obvious. For example, the GC flame photometric method for the determination of mustard gas in soils has reached a limit of quantification of 0.05 mg/kg, but it is still higher than the upper limit of the allowable residual concentration of 0.02 mg/kg regulated by Chinese environmental standards [5]. The portable Fourier transform infrared spectrometer needs standard samples for calibration, and liquid chromatography requires a longer time and has specific requirements for the choice of detector and analytical column, and so on [5]. In comparison with instrumental analysis, systems based on chromogenic and fluorogenic methods are much simpler and easier to operate [6]. However, the design and development of fluorescence sensors with high-accuracy and sensitivity are very challenging because of the absence of traditional probing recognition sites and weak electrophilicity of **SM**. Successful examples demonstrating that fluorescence sensors can identify **SM** and its simulants remain exceedingly rare. Until now, only a few elegant optical probes have successfully detected **SM** and its analogs [7]. For example, Kumar and Anslyn developed a chemosensor for **SM** by executing a metal-ion indicator displacement assay in 2013 [8]. Recently, our group reported an AIE-active tetraphenylethene chemodosimeter for **SM** stimulants [9]. However, both these two systems are based on the reaction of benzenemethanethiol with **SM** and exhibited a high response temperature (80 °C). In 2014, the Pardasani group developed a rhodamine-based fluorescence probe for **SM**, utilizing a spirothiolactam ring opening followed by a desulfurization reaction of rhodamine-thioamide with **SM** [10]. This method is refreshing, but exhibited a long response time for **SM** at room temperature (1 h). The development of new colorimetry or fluorometry-based chemosensors that meet the criteria of simplicity, rapidity, and on-site analysis of **SM** is still highly desired.

Rhodol (or rhodafluor), which can be regarded as a mixture of rhodamine and fluorescein, exhibits many excellent photophysical

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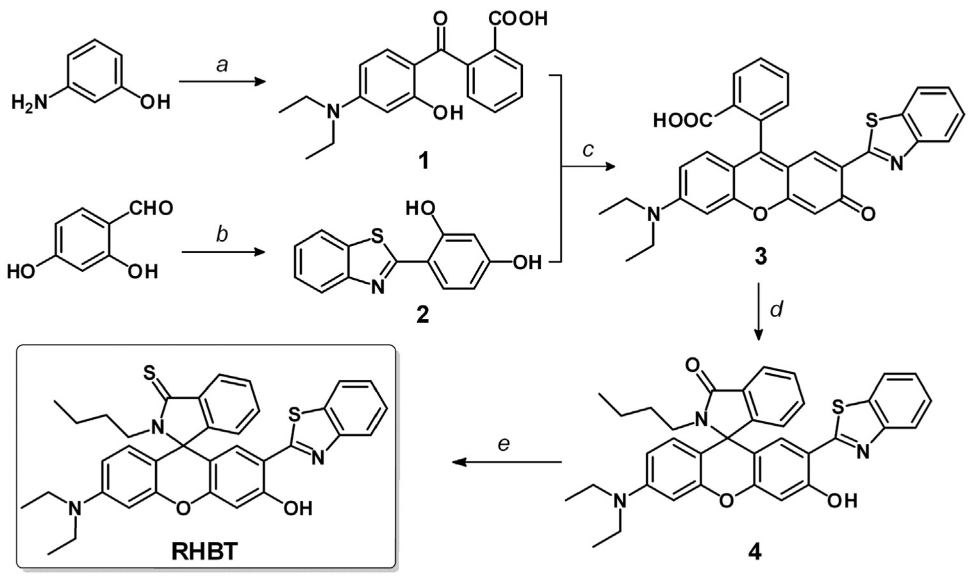
https://doi.org/10.1016/j.talanta.2018.06.066
Received 25 April 2018; Received in revised form 12 June 2018; Accepted 20 June 2018



Scheme 1. Synthesis of the Probe RHBT. Reagents and conditions: (a) bromoethane, sodium carbonate, ethanol, rt, 72 h; phthalic anhydride, toluene, reflux, 10 h, NaOH/HCl, 82%; (b) 2-aminothiophenol, sodium metabisulfite, DMF, reflux, 2 h, 50.0%; (c) methanesulfonic acid, 90 °C, 24 h, 54%; (d) *n*-butylamine, ethanol, reflux, 24 h, 42%; (e) P_2S_5, dry toluene, 80 °C, 1 h, 55%.

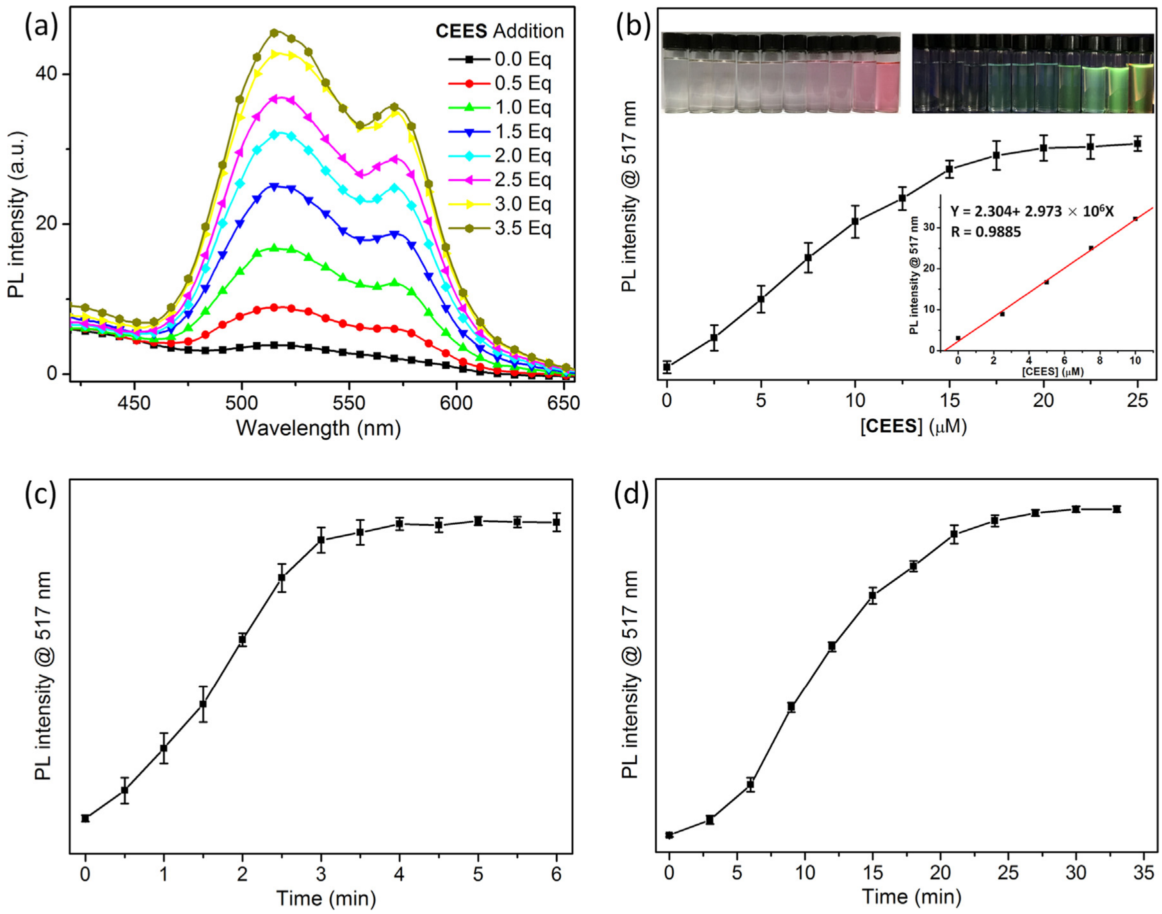


Fig. 1. (a) Fluorescence titration of a methanol solution of **RHBT** (5.0 μM) with increasing concentration of **CEES**. (b) The relationship of the fluorescence intensity of **RHBT** at 517 nm and **CEES** concentration respectively, inset: colorimetric and fluorogenic responses of **RHBT** solution with sequential addition of **CEES** from left to right. (c) Reaction-time profiles: the fluorescence intensity of the reaction solution of **RHBT** (5.0 μM) with 4.0 equivalents of **CEES** at 60 °C at 517 nm versus time (within 6 min) and (d) at room temperature (within 35 min).

properties, i.e., high photostability, high fluorescence quantum yield and good solubility [11]. Recently, rhodol derivatives have been reported as fluorescent sensors due to the ring-opening reactions from the nonfluorescent spirocycle form to the strongly fluorescent quinoid form upon appropriate external stimuli [12]. The rhodamine-based sensor for **SM** reported by Pardasani exhibited a slow response for **SM** at room temperature, which resulted from the slow ring-opening reactions of rhodamine [10a]. We considered that when using rhodol as the mainstay of the probe molecule, and connecting a benzothiazole fragment at a position *ortho* to the hydroxyl group of rhodol (Scheme 1), it will form