Sensors and Actuators B 234 (2016) 27–33

Contents lists available at ScienceDirect

Sensors and Actuators B: Chemical

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

A red-emitting fluorescent probe for specific detection of cysteine over homocysteine and glutathione with a large Stokes shift

Xingjiang Liu[a,1], Dalei Yang[a,1], Wenqiang Chen[a], Lei Yang[a], Fengpei Qi[a], Xiangzhi Song[a,b,c,*]

[a] College of Chemistry & Chemical Engineering, Central South University, Changsha, Hunan Province 410083, PR China
[b] State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian, Liaoning Province 116024, PR China
[c] Key Laboratory of Resource Chemistry of Nonferrous Metals, Ministry of Education 932 Lushan South Road, Changsha, Hunan Province 410083, PR China

ARTICLE INFO

Article history:
Received 13 January 2016
Received in revised form 22 April 2016
Accepted 25 April 2016
Available online 26 April 2016

Keywords:
Fluorescence
Probe
Cysteine (Cys)
Large Stokes shift
Red-emitting

ABSTRACT

A red-emitting fluorescent probe for selective detection of cysteine was developed based on the conjugated addition/cyclization sequence mechanism. Upon the treatment with cysteine, this probe exhibits a strong fluorescence enhancement (62-fold) and a large Stokes shift (148 nm). The detection limit was calculated to be as low as 6.6 nM based on S/N = 3. Importantly, the practical application of this probe for the selective detection of cysteine was successfully demonstrated in living cells.

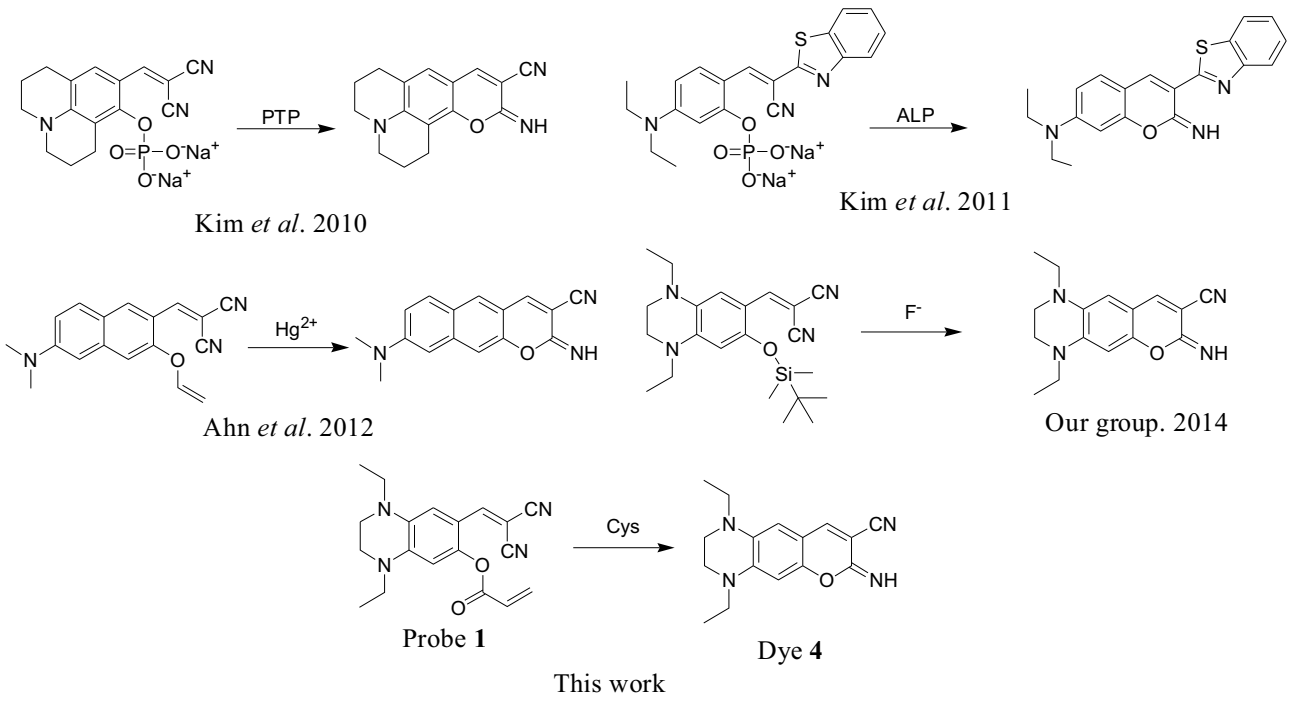
1. Introduction

Biothiols, such as cysteine (Cys), homocysteine (Hcy) and glutathione (GSH), play crucial roles in mediating a number of physiological and pathological processes in mammalian system [1–3]. Numerous investigations have demonstrated that the abnormal levels of these biothiols are closely associated with many diseases. Cys deficiency is related to the slowed growth, liver damage, hair depigmentation, skin lesions, lethargy and edema [4]. The study found that elevated Hcy in plasma is involved in cardiovascular disease, Alzheimer's disease and osteoporosis [5,6]. GSH has the protective ability against oxidative and free-radical-mediated injury and closely linked to leucocyte loss, cancer, HIV infection, etc. Thus, the level of GSH serves as an indicator to evaluate the redox state and detoxification status in organism [7–9]. Therefore, it's important to develop efficient methods for the selective and sensitive detection of biotiols, particularly those that can distinguish these three species. Due to its advantages of the operational simplicity, non-invasiveness, high sensitivity, and high spatial and temporal resolution, fluorescence sensing is a preferred choice for the detection of biothiols [10–17].

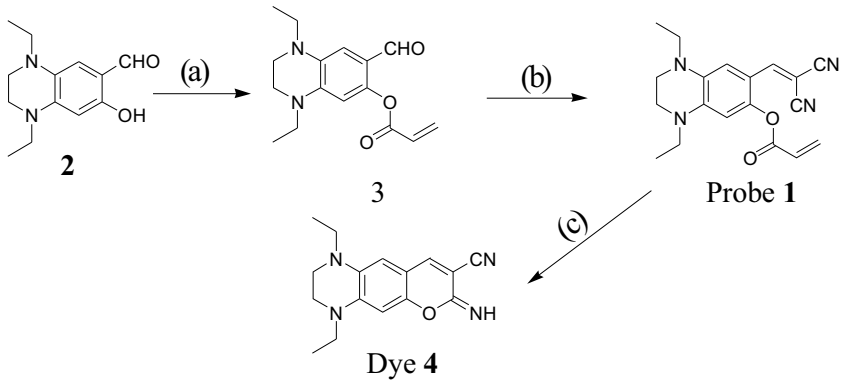
In the past decade, a large number of fluorescent probes for biothiols have been reported [18–24]. Although these probes display good selectivity toward biothiols over other amino acids, most of them can't distinguish these three biothiols. Because GSH, Cys and Hcy have close correlations between each other, it's very meaningful if the fluorescent probe can discriminate one of them. However, it's challenging to develop fluorescent probes for discriminatory detection of these three biothiols due to their similar structure and reactivity. In the selective detection of Cys from GSH, Hcy and other amino acids, the conjugate addition/cyclization of Cys to acrylate moiety has proven to be an effective strategy, which has been successfully demonstrated in typical chromophores such as fluorescein [13,25], naphthalimide [26], coumarin [27], cyanine [28], HBT [29], and others [30]. While being valuable, it's noteworthy that most of these reported probes showed short emission wavelengths (<600 nm) or relatively small Stokes shifts (<100 nm). It's well known that long wavelength used in fluorescence detection can reduce the background interference and photo-damage to living cells [31–34]. Moreover, fluorescent dyes with large Stokes shifts can improve the detection sensitivity by avoiding fluorescence quenching induced by self-absorption and fluorescence errors caused by the excitation back scattering effect [35,36]. To date, there is no acrylate-based fluorescent probe reported having both an emission in red/NIR region and a large Stokes shift for specific detection of Cys.

* Corresponding author.
E-mail address: song@rowland.harvard.edu (X. Song).
[1] These authors contribute equal to this work.

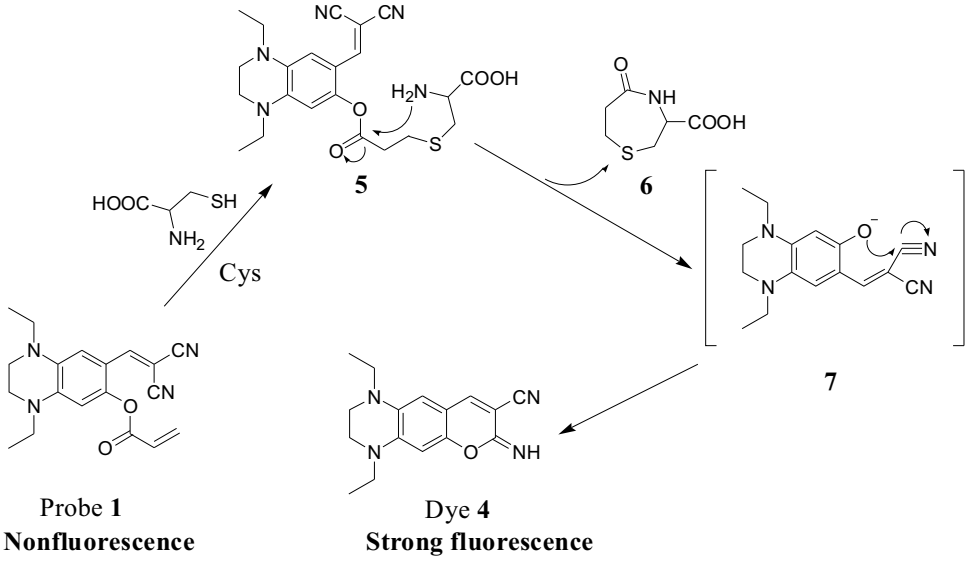
http://dx.doi.org/10.1016/j.snb.2016.04.141
0925-4005/



Scheme 1. Iminocoumarin-based fluorescent probes and dyes.



Scheme 2. Synthetic route of Probe **1**. (a) Acryloyl chloride, DCM, triethylamine, r.t., 1 h, yield 87.5%. (b) Malononitrile, Triethylamine, DCM, r.t., 30 min, yield 10%. (c) Cys, CH_3CN/HEPES buffer (pH = 7.4), r.t., 1 h, yield 31%.



Scheme 3. Proposed sensing mechanism of Probe **1** in response to Cys.