Synthesis and characterizations of a highly sensitive and selective fluorescent probe for hydrogen sulfide

Yan Huang, Changyu Zhang, Zhen Xi, Long Yi

PII: S0040-4039(16)30127-7
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.02.017
Reference: TETL 47290

To appear in: *Tetrahedron Letters*

Received Date: 22 November 2015
Revised Date: 30 January 2016
Accepted Date: 3 February 2016

Please cite this article as: Huang, Y., Zhang, C., Xi, Z., Yi, L., Synthesis and characterizations of a highly sensitive and selective fluorescent probe for hydrogen sulfide, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.02.017

ELSEVIER

Tetrahedron Letters

journal homepage: www.elsevier.com

Synthesis and characterizations of a highly sensitive and selective fluorescent probe for hydrogen sulfide

Yan Huang[a,†], Changyu Zhang[a,†], Zhen Xi[b,*], Long Yi[a,*]

[a]*State Key Laboratory of Organic-Inorganic Composites, Beijing University of Chemical Technology, Beijing 100029, China. E-mail: yilong@mail.buct.edu.cn*

[b]*State Key Laboratory of Elemento-Organic Chemistry and Department of Chemical Biology, National Pesticide Engineering Research Center (Tianjin), Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Nankai University, Tianjin, 300071, China. E-mail: zhenxi@nankai.edu.cn*

[†] *The authors pay equal contributions to this work.*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Bioimaging
Fluorescence probe
Hydrogen sulfide
NBD amine
Thiolysis

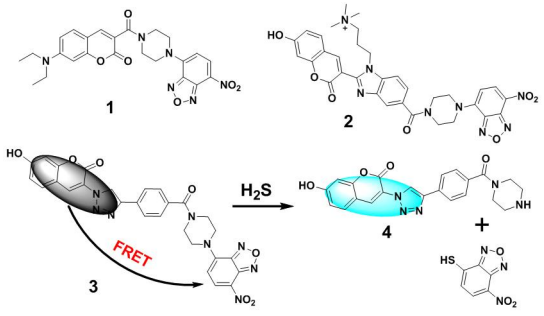
ABSTRACT

Hydrogen sulfide (H_2S) is an important endogenous signaling molecule with a variety of biological functions. To detect H_2S in living biological systems, herein we developed a new fluorescent probe for highly sensitive and selective sensing of H_2S in cells. The probe is based on coumarin-triazole as the fluorophore and thiolysis of the NBD (7-nitro-1,2,3-benzoxadiazole) amine as the receptor. Bioimaging experiments indicated that this probe could be used to monitor H_2O_2-induced H_2S biosynthesis in yeast cells. Our results show that such thiolysis of the NBD amine can be used for development of fluorescent H_2S probes.

Introduction

Hydrogen sulfide (H_2S) is an important endogenous signalling molecule with significantly biological functions.[1-3] The production of endogenous H_2S in different organs and tissues has been majorly attributed to three distinctive enzymatical pathways including cystathionine β-synthase (CBS), cystathionine γ-lyase (CSE) and 3-mercaptopyruvate sulfur transferase (3-MPST) coupling with cysteine aminotransferase (CAT).[2] It has been proved that abnormal endogenous level of H_2S relates to numerous human diseases, including symptoms of Alzheimer's disease, Down syndrome, diabetes and liver cirrhosis.[3] Moreover, H_2S is proposed to play important roles in mediating a wide range of physiological processes, such as neurotransmission, vasodilation, inflammation, oxygen sensing, etc.[4] Although those studies indicated that numerous physiological and pathological processes were linked to levels of H_2S, the molecular mechanisms dictating how H_2S influences cellar signaling and interrelated biological events were insufficient understood. Therefore, it presents significant research value to develop efficient methods for detection of H_2S in biological systems.

Traditionally, the main methods for H_2S detection are colorimetry, electrochemical assay, gas chromatography and sulfide precipitation.[5] However, recent research indicated that fluorescent methods with excellent sensitivity and selectivity were highly desirable for *in situ* and real-time visualization of H_2S in living biological systems.[6-11] These H_2S probes are mostly based on specific H_2S-induced reactions, including reduction-based probes,[6-8] metal sulfide precipitation-based probes[9] and nucleophile-based probes.[10] We have been interested in the biodetection of H_2S[11] and biothiols[12] for some time. In our previous work, the thiolysis of the NBD (7-nitro-1,2,3-benzoxadiazole) amine was explored for development of a FRET-based H_2S probe **1** (Scheme 1),[11a] which displayed good selectivity for H_2S over biothiols or SO_3^{2-}. However, Roubinet[13] et al. recently reported another NBD-amine-based probe **2** (Scheme 1) which 1) possessed no selectivity for S^{2-} and SO_3^{2-} and 2) could only react with Na_2S, but not NaHS in their tests.[13] To further investigate such thiolysis of the NBD amine for development of fluorescent H_2S probes, herein we reported the synthesis and characterizations of a new NBD-based probe **3**, which could be used to detect H_2S selectively and to monitor the H_2O_2-induced H_2S biosynthesis in yeast cells.



Scheme 1. Chemical structures of NBD-based fluorescent probes **1**-**3** and the reaction of **3** and H_2S to produce **4**.

Herein, we developed a new NBD-based fluorescent probe **3** based on click reaction of alkyne-containing NBD **7** and