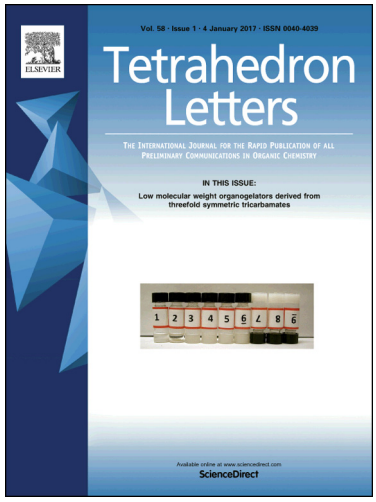


Highly Selective Fluorescent Recognition of Glutathione by Using a Water Soluble Binaphthyl Aldehyde

Wei Chen, Xuedan Wu, Lin Pu

PII: S0040-4039(17)30395-7
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.03.074
Reference: TETL 48775

To appear in: *Tetrahedron Letters*

Received Date: 22 February 2017
Revised Date: 23 March 2017
Accepted Date: 24 March 2017

Please cite this article as: Chen, W., Wu, X., Pu, L., Highly Selective Fluorescent Recognition of Glutathione by Using a Water Soluble Binaphthyl Aldehyde, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.03.074

Highly Selective Fluorescent Recognition of Glutathione by Using a Water Soluble Binaphthyl Aldehyde

Wei Chen, Xuedan Wu and Lin Pu*

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22904-4319, U.S.A.

Email Address: lp6n@virginia.edu

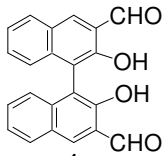
Abstract

A water soluble binaphthyl-based aldehyde was designed and synthesized. This compound in combination with $Zn(OAc)_2$ is found to exhibit greatly enhanced fluorescence in the presence of GSH in aqueous solution (pH = 7.5) but give little or no fluorescence enhancement in the presence of cysteine, homocysteine and other amino acids. This remarkable selectivity makes this probe potentially useful for the analysis of the biologically important GSH.

Keywords: Fluorescence sensor Glutathione Zinc BINOL Aldehyde

Intracellular thiols including glutathione (GSH), cysteine (Cys) and homocysteine (Hcy) play important roles in physiological and pathological processes, and extensive studies have been conducted to detect these molecule.[1-3] Utilizing the nucleophilic reactions of the thiols has led to the development of a number of fluorescent sensor for GSH, Cys and Hcy.[1-3] However, to distinguish these biologically significant thiols from each other has become a challenge. Although several reports have appeared for the selective fluorescent detection of GSH,[4-7] research on the development of more selective and efficient fluorescent sensors continues.

In 2014, we discovered that the 1,1'-bi-2-naphthol (BINOL)-based aldehyde **1** in combination with Zn^{2+} exhibits enantioselective fluorescent enhancement in the presence of chiral amines in methanol solution.[8] In order to explore the application of the BINOL-based molecules for the fluorescent detection of biologically important molecules in water solution, we have synthesized a water soluble analog of this compound. Herein, we report that a highly selective fluorescent sensor for GSH by using the BINOL-based compound in aqueous solution.



1

In order to make the BINOL-based aldehyde soluble in water, we have incorporated a quaternary ammonium cation as shown in Scheme 1. Compound **2** was prepared from (*S*)-BINOL according to the literature.[9] Treatment of **2** sequentially with 1,3-dibromopropane and morphline under basic conditions gave **3**. Ortho-metalation of **3** with ^{n}BuLi followed by addition of DMF and acidic deprotection gave the BINOL-aldehyde compound **4**. Reaction of **4** with MeI gave the desired quaternary ammonium salt **5** which is found to be soluble in aqueous solution.[10] In DMSO-d_6 solution, compound **5** gave two ^{1}H NMR signals at δ 10.36 (s, 1H) and 10.15 (s, 1H) which are assigned to the signals of the aldehyde and hydroxyl protons respectively. In D_2O solution, the aldehyde proton signal was observed at δ 10.24 while the phenol proton disappeared by H/D exchange.