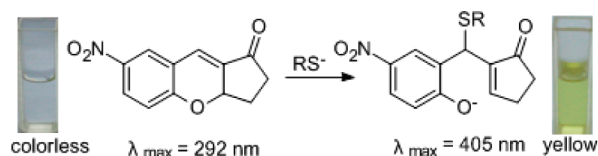


Colorimetric Detection of Thiols Using a  
Chromene MoleculeFang-Jun Huo,<sup>†</sup> Yuan-Qiang Sun,<sup>†</sup> Jing Su,<sup>‡</sup> Jian-Bin Chao,<sup>†</sup> Hai-Juan Zhi,<sup>‡</sup> and  
Cai-Xia Yin<sup>\*‡</sup>*Research Institute of Applied Chemistry (RIAC), Key Laboratory of Chemical Biology  
and Molecular Engineering of Ministry of Education, Institute of Molecular Science  
(IMS), Shanxi University, Taiyuan, 030006, China*

yincx@sxu.edu.cn

Received August 31, 2009

## ABSTRACT



A new thiol-containing colorimetric probe has been developed by using a chromene derivative, 7-nitro-2,3-dihydro-1H-cyclopenta[b]chromen-1-one (1). The molecule exhibited high selectivity and sensitivity for detecting thiol species as cysteine, homocysteine, and glutathione in aqueous solution through a rapid visual color change from colorless to yellow.

Thiol-containing amino acids and peptides play crucial roles in many physiological processes. For example, cysteine (Cys) and homocysteine (Hcy) are considered to be related to a number of health disorders such as renal failure,<sup>1</sup> AIDS,<sup>2</sup> Alzheimer's and Parkinson's diseases,<sup>3</sup> atherosclerotic cardiovascular diseases,<sup>4</sup> neutral tube defects, and coronary heart disease.<sup>5</sup> Glutathione (GSH), an important tripeptide with a thiol group, performs vital biological functions that are involved in combating oxidative stress and maintaining redox homeostasis.<sup>6</sup> Thus, the rapid, sensitive, and selective detection of thiols is of considerable importance and significant interest. Many assays have been carried out, including high

performance liquid chromatography,<sup>7</sup> capillary electrophoresis,<sup>8</sup> UV–vis detection,<sup>9</sup> electrochemical detection,<sup>10</sup> fluorescence detection,<sup>11</sup> mass spectrometry identification,<sup>12</sup> colorimetric assays,<sup>13</sup> and others.<sup>14</sup> Most recently, several coumarin derivatives were reported to detect biological thiols.<sup>15</sup> These results stimulated us to explore whether chromene (which is similar to coumarin in structure) derivatives might act as a probe to detect thiol-containing molecules. Herein, we report a novel colorimetric probe for thiol-containing amino acids and peptides in aqueous solution by

<sup>†</sup> RIAC.<sup>‡</sup> IMS.(1) Sofia, C.; Chadeaux, B.; Coude, M.; Oaillard, O.; Kamoun, E. *Clin. Chem.* **1990**, *36*, 2137–2138.(2) Staal, F. J. T.; Ela, S. W.; Roederer, M.; Anderson, M. T.; Herzenberg, L. A. *Lancet* **1992**, *339*, 909–912.(3) Heafield, M. T.; Fearn, S.; Steventon, G. B.; Waring, R. H.; Williams, A. C.; Sturman, S. G. *Neurosci. Lett.* **1990**, *110*, 216–220.(4) (a) Nygard, O.; Nordrehaug, J. E.; Refsum, H.; Ueland, P. M.; Farstad, M.; Vollset, S. E. *N. Engl. J. Med.* **1997**, *337*, 230–237. (b) Jacobsen, D. W. *Clin. Chem.* **1998**, *44*, 1833–1843.(5) Seshadri, S.; Beiser, A.; Selhub, J.; Jacques, P. F.; Rosenberg, I. H.; Agostino, R. B.; Wilson, P. W. F.; Wolf, P. A. *N. Engl. J. Med.* **2002**, *346*, 476–483.(6) Pullella, P. K.; Chiku, T.; Carvan, M. J., III.; Sem, D. S. *Anal. Biochem.* **2006**, *352*, 265–273.(7) (a) Ellman, G. L. *Arch. Biochem. Biophys.* **1959**, *82*, 70–77. (b) Komuro, C.; Ono, K.; Shibamoto, Y.; Nishidai, T.; Takahashi, M.; Abe, M. *J. Chromatogr.* **1985**, *338*, 209–212. (c) Chen, W.; Zhao, Y.; Seefeldt, T.; Guan, X. *J. Pharm. Biomed. Anal.* **2008**, *48*, 1375–1380.(8) (a) Inoue, T.; Kirchhoff, J. R. *Anal. Chem.* **2000**, *72*, 5725–5730. (b) Zinellu, A.; Sotgia, S.; Scanu, B.; Usai, M. F.; Fois, A. G.; Spada, V.; Deledda, A.; Deiana, L.; Pirina, P.; Carru, C. *Amino Acids* **2009**, *37*, 395–400.(9) (a) Zhu, J.; Dhimitruka, L.; Pei, D. *Org. Lett.* **2004**, *6*, 3809–3812. (b) Potesil, D.; Petrlova, J.; Adam, V.; Vacek, J.; Klejdus, B.; Zehnalek, J.; Trnkova, L.; Havel, L.; Kizek, R. *J. Chromatogr. A* **2005**, *1084*, 134–144. (c) Fei, S. D.; Chen, J. H.; Yao, S. Z.; Deng, G. H.; He, D. L.; Kuang, Y. F. *Anal. Biochem.* **2005**, *339*, 29–35.(10) (a) Amarnath, K.; Amarnath, V.; Amarnath, K.; Valentine, H. L.; Valentine, W. M. *Talanta* **2003**, *60*, 1229–1238. (b) Wen, M.; Liu, H.; Zhang, F.; Zhu, Y.; Liu, D.; Tian, Y.; Wu, Q. *Chem. Commun.* **2009**, 4530–4532.

employing a chromene derivative, 7-nitro-2,3-dihydro-1*H*-cyclopenta[*b*]chromen-1-one (**1**)<sup>16</sup> (Scheme 1, as well as

**Scheme 1**

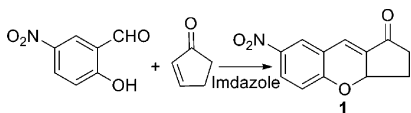


Figure S1 in the Supporting Information), which was prepared by the reaction of 5-nitrosalicylaldehyde and

(11) (a) Duan, L.; Xu, Y.; Qian, X.; Wang, F.; Liu, J.; Cheng, T. *Tetrahedron Lett.* **2008**, *49*, 6624–6627. (b) Shibata, A.; Furukawa, K.; Abe, H.; Tsuneda, S.; Ito, Y. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2246–2249. (c) Matsumoto, T.; Urano, Y.; Shoda, T.; Kojima, H.; Nagano, T. *Org. Lett.* **2007**, *9*, 3375–3377. (d) Piggott, A. M.; Karuso, P. *Anal. Chem.* **2007**, *79*, 8769–8773. (e) Bouffard, J.; Kim, Y.; Swager, T. M.; Weissleder, R.; Hilderbrand, S. A. *Org. Lett.* **2008**, *10*, 37–40. (f) Huang, S. T.; Ting, K. N.; Wang, K. L. *Anal. Chim. Acta* **2008**, *620*, 120–126. (g) Fu, Y.; Li, H.; Hu, W.; Zhu, D. *Chem. Commun.* **2005**, 3189–3191. (h) Maeda, H.; Matsuno, H.; Ushida, M.; Katayama, K.; Saeki, K.; Itoh, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 2922–2925. (i) Zhang, M.; Li, M.; Zhao, Q.; Li, F. Y.; Zhang, D. Q.; Zhang, J. P.; Yi, T.; Huang, C. H. *Tetrahedron Lett.* **2007**, *48*, 2329–2333. (j) Chow, C. F.; Chiu, B. K. W.; Lam, M. H. W.; Wong, W. Y. *J. Am. Chem. Soc.* **2003**, *125*, 7802–7803. (k) Tanaka, F. J.; Mase, N.; Barbas, C. F., III. *Chem. Commun.* **2004**, 1762–1763.

(12) (a) Burford, N.; Eelman, M. D.; Mahony, D. E.; Morash, M. *Chem. Commun.* **2003**, 146–147. (b) Fafii, M.; Elango, R.; Courtney-Martin, G.; House, J. D.; Fisher, L.; Pencharz, P. B. *Anal. Biochem.* **2007**, *371*, 71–81.

(13) (a) Zeng, Y.; Zhang, G.; Zhang, D. *Anal. Chim. Acta* **2008**, *627*, 254–257. (b) Guo, Y.; Shao, A.; Xu, J.; Shi, Y.; Jiang, S. *Tetrahedron Lett.* **2004**, *45*, 6477–6480. (c) Zhang, X.; Li, C.; Cheng, X.; Wang, X.; Zhang, B. *Sens. Actuators, B* **2008**, *129*, 152–157. (d) Caroen, L.; Eycken, J. V. D. *Tetrahedron Lett.* **2009**, *50*, 41–44. (e) Ros-Lis, J. V.; Garcia, B.; Jimenez, D.; Martinez-Manez, R.; Sancenon, F.; Soto, J.; Gonzalvo, F.; Valdecabres, M. C. *J. Am. Chem. Soc.* **2004**, *126*, 4064–4065. (f) Yang, S. J.; Tian, X. Z.; Shin, I. *Org. Lett.* **2009**, *11*, 3438–3441. (g) Rusin, O.; Luce, N. S.; Agbaria, R. A.; Escobedo, J. O. S.; Jiang, I.; Warner, M.; Dawan, F. B.; Lian, K.; Strongin, R. M. *J. Am. Chem. Soc.* **2004**, *126*, 438–439. (h) Wang, W.; Rusin, O.; Xu, X.; Kim, K. K.; Escobedo, J. O.; Fakayode, S. O.; Fletcher, K.; Lowry, A. M.; Schowalter, C. M.; Lawrence, C. M.; Fronczek, F. R.; Warner, I. M.; Strongin, R. M. *J. Am. Chem. Soc.* **2005**, *127*, 15949–15958. (i) Zhang, D. Q.; Zhang, M.; Liu, Z. Q.; Yu, M. X.; Li, F. Y.; Yi, T.; Huang, C. H. *Tetrahedron Lett.* **2006**, *47*, 7093–7096. (j) Wang, W. H.; Escobedo, J. O.; Lawrence, C. M.; Strongin, R. M. *J. Am. Chem. Soc.* **2004**, *126*, 3400–3401. (k) Han, M. S.; Kim, D. H. *Tetrahedron* **2004**, *60*, 11251–11257. (l) Shao, N.; Jin, J. Y.; Cheung, S. M.; Yang, R. H.; Chan, W. H.; Mo, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4944–4948.

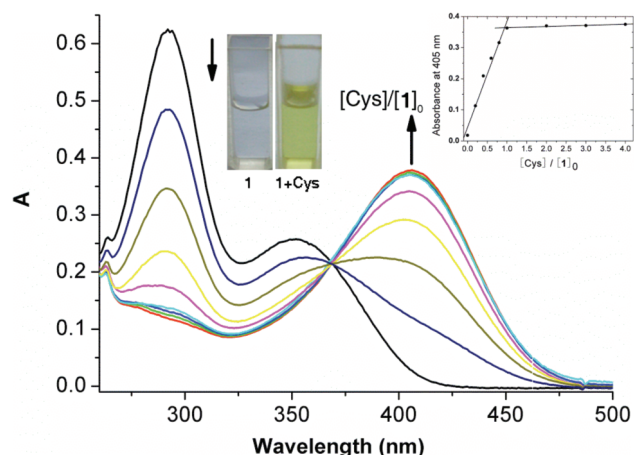
(14) (a) Badyal, J. P.; Cameron, A. M.; Cameron, N. R.; Coe, D. M.; Cox, R.; Davis, B. G.; Oates, L. J.; Oye, G.; Steel, P. G. *Tetrahedron Lett.* **2001**, *42*, 8531–8533. (b) Zacharis, C. K.; Tzanavaras, P. D.; Themelis, D. G. *J. Pharm. Biomed. Anal.* **2009**, *50*, 384–391.

(15) (a) Lee, K. S.; Kim, T. K.; Lee, J. H.; Kim, H. J.; Hong, J. I. *Chem. Commun.* **2008**, 6173–6175. (b) Kim, T. K.; Lee, J. H.; Kim, H. J. *Tetrahedron Lett.* **2008**, *49*, 4879–4881. (c) Lin, W.; Yuan, L.; Cao, Z.; Feng, Y.; Long, L. *Chem.—Eur. J.* **2009**, *15*, 5096–5103. (d) A latest fluorescent thiol probe was reported by Xi groups using a coumarin derivative where the kinetic study was carried under 1000-fold thiol to their probe: Yi, L.; Li, H.; Sun, L.; Liu, L.; Zhang, C.; Xi, Z. *Angew. Chem., Int. Ed.* **2009**, *48*, 4034–4037. (e) Hong, V.; Kislukhin, A. A.; Finn, M. G. *J. Am. Chem. Soc.* **2009**, *131*, 9986–9994.

(16) The probe **1** molecule: <sup>1</sup>H NMR (300 MHz, 25 °C, CDCl<sub>3</sub>) δ 8.14 (m, 2H), 7.18 (s, 1H), 6.98 (d, 1H), 5.37 (t, 1H), 2.15–2.40 (m, 2H), 2.58–2.80 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 24.25, 33.00, 113.31, 117.96, 121.58, 121.88, 123.80, 138.69, 156.24, 196.37. Elemental anal. (calcd %) for C<sub>12</sub>H<sub>9</sub>NO<sub>4</sub>: C, 62.34; H, 6.06; N, 3.92. Found: C, 62.78; N, 6.01; H, 4.01. Crystal data for **1**: C<sub>12</sub>H<sub>9</sub>NO<sub>4</sub>, FW = 231.2, crystal size: 0.2 × 0.2 × 0.1 mm, monoclinic, space group *P2<sub>1</sub>/n* (No. 14), *a* = 6.0584(11) Å, *b* = 19.717(4) Å, *c* = 8.9513(16) Å, β = 98.257(4)°, *V* = 1058.2(3) Å<sup>3</sup>, *Z* = 4, *T* = 293 K, θ<sub>max</sub> = 25.0°, 4356 reflections measured, 1850 unique (*R*<sub>int</sub> = 0.0412). Final residual for 183 parameters and 1165 reflections with *I* > 2σ(*I*): *R*<sub>1</sub> = 0.0524, *wR*<sub>2</sub> = 0.11247, and GOF = 0.98. Huo, F. J.; Yin, C. X.; Yang, P. 7-Nitro-2,3-dihydro-1*H*-cyclopenta[*b*]chromen-1-one. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2004**, *60*, o2087–o2089.

2-cyclohexen-1-one via Baylis–Hillman and intramolecular Michael addition in the presence of imidazole.

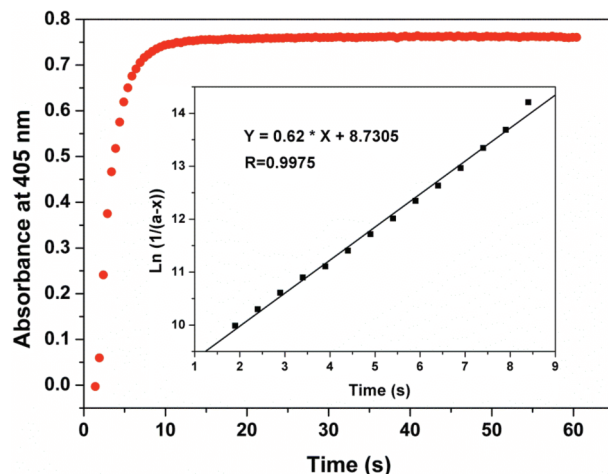
Figure 1 shows the change in the UV/visible spectrum when the cysteine solution is added to HEPES buffer (10



**Figure 1.** Absorption spectral changes of **1** (25 μM) in HEPES 10 mM containing 0.1% EtOH, pH 7.0 aqueous buffer upon addition of cysteine; cysteine was added gradually with [Cys] = 0, 5, 10, 15, 20, 25, 50, 75, and 100 μM. Each spectrum is recorded 2 min after cysteine addition. Inset: Absorbance at 405 nm as a function of Cys concentration, indicating a 1:1 ratio for cysteine and probe **1**.

mM, pH 7.0) containing probe **1** (25 μM). With increasing Cys concentration, the probe **1** absorption peak at 292 nm is gradually decreased and a new peak appears at 405 nm (red-shifted 113 nm) with an isosbestic point at 368 nm, indicating the formation of a new compound. The stoichiometric ratio between probe **1** and Cys was found to be 1:1 based on the change of the absorbance at 405 nm (inset in Figure 1) to concentration of Cys.

Figure 2 shows the kinetic study of the response of cysteine to probe **1** under pseudo-first-order conditions (50



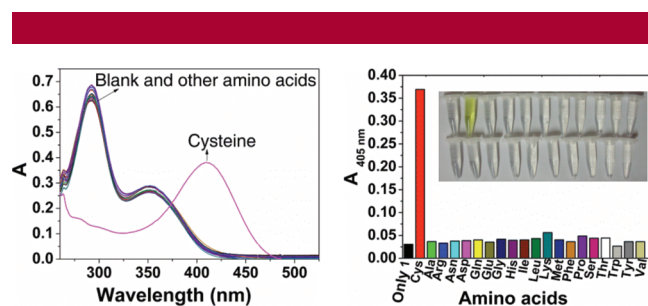
**Figure 2.** The kinetic study of the response of the probe **1** to Cys at 25 °C under pseudo-first-order condition ([**1**] = 50 μM, [Cys] = 500 μM).

$\mu\text{M}$  probe **1** and  $500\ \mu\text{M}$  cysteine). The reaction was finished within 10 s. Rate constants were obtained by fitting the initial concentration change (5–90%) according to a pseudo-first-order kinetics equation. The observed rate constant at pH 7.0 and  $25\ ^\circ\text{C}$  was  $k_{\text{obs}} = 0.62\ \text{s}^{-1}$ ,  $t_{1/2} = 1.0\ \text{s}$ , indicating that probe **1** can react rapidly with cysteine under these experimental conditions.

The pH range (5.0–10.0) for determination of cysteine was also studied and the result showed that the system had the above-mentioned UV/visible light absorption with no significant difference within the pH range 7.0–10.0 (Figure S2, see Supporting Information). We therefore selected the physiological condition of a HEPES 10 mM, pH 7.0 buffer aqueous solution. Systems with  $\text{pH} < 7.0$  will not exhibit a notable change in either color or UV/visible spectrum.

The system exhibited higher selectivity toward Cys than other amino acids, including L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-glutamine, L-glutamic acid, L-glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine, and L-valine.

Figure 3 left displays a series of UV/visible spectra changes when common amino acids (in large excess, 10



**Figure 3.** (Left) UV/vis absorption spectra of the probe **1** ( $25\ \mu\text{M}$ ) in pH 7.0 aqueous buffer (HEPES 10 mM containing 0.1% EtOH) solution in the presence of  $250\ \mu\text{M}$  other amino acids including Ala, Arg, Asn, Asp, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, and Val. [Cys] =  $25\ \mu\text{M}$ . (Right) Optical density of the probe **1** ( $25\ \mu\text{M}$ ) at 405 nm upon addition of amino acids. Inset: A color change photograph for Cys and other amino acids.

equiv to Cys) were added into a 10 mM HEPES buffer solution containing  $25\ \mu\text{M}$  of probe **1**. Only Cys caused an apparent red shift from 292 to 405 nm. When changes at 405 nm were monitored, good selectivity was observed for Cys with a more than 10-fold intensity increase in absorbance (Figure 3 right). The effect caused by Cys was very significant and a distinct color change from colorless to yellow could be detected by the naked eye, while the color of the solutions containing the other amino acids remained relatively unchanged (Figure 3 right inset). This indicates that the addition of other amino acids to the probe **1** system altered neither the color nor the UV–vis spectra in the system, nor did their presence interfere with the detection of Cys. The above results are very useful for biological analysis due to the method’s simplicity, speed, and use of uncomplicated apparatus.

Simultaneously, anions with physiological functions were excluded, including fluoride ( $\text{F}^-$ ), chloride ( $\text{Cl}^-$ ), bromide ( $\text{Br}^-$ ), iodide ( $\text{I}^-$ ), acetate ( $\text{AcO}^-$ ), thiocyanate ( $\text{SCN}^-$ ), nitrate ( $\text{NO}_3^-$ ), sulfate ( $\text{SO}_4^{2-}$ ), carbonate ( $\text{CO}_3^{2-}$ ), oxalate ( $^-\text{OOC}\text{COO}^-$ ), and phosphate ( $\text{PO}_4^{3-}$ ) which did not interfere with the determination of thiols (Figure S3, see the Supporting Information). This is very positive for the detection of thiols in biological samples such as urine or serum.

The effect of a wide range of environmentally and physiologically important metal ions on the UV–vis spectrum was investigated by preparing solutions containing **1** ( $25\ \mu\text{M}$ ) and the ion ( $25\ \mu\text{M}$ ). The result showed that different metal ions have different inhibition effects. The common metal ions such as  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Ba}^{2+}$ ,  $\text{V}^{4+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Al}^{3+}$ ,  $\text{Ga}^{3+}$ ,  $\text{Sn}^{2+}$ ,  $\text{Zr}^{4+}$ ,  $\text{Ce}^{3+}$ ,  $\text{Nd}^{3+}$ ,  $\text{Sm}^{3+}$ ,  $\text{Eu}^{3+}$ ,  $\text{Er}^{3+}$ ,  $\text{Tb}^{3+}$ ,  $\text{Ho}^{3+}$ , and  $\text{Yb}^{3+}$  did not affect the detection, whereas the probe system could be partly or completely inhibited by equivalent molar concentrations of  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Cu}^{2+}$ , or  $\text{Hg}^{2+}$  due to the formation of coordinate complexes between these ions and cysteine. For these metal ions, when a strong chelator, EDTA (1:1 to  $\text{M}^{2+}$ ), was hired to shield them, the probe system could resume its probing thiol performance with the exception only of  $\text{Hg}^{2+}$  ions (Figure S4, Supporting Information). Therefore, these would not hinder the reported chromene molecule in use as a successful thiol probe.

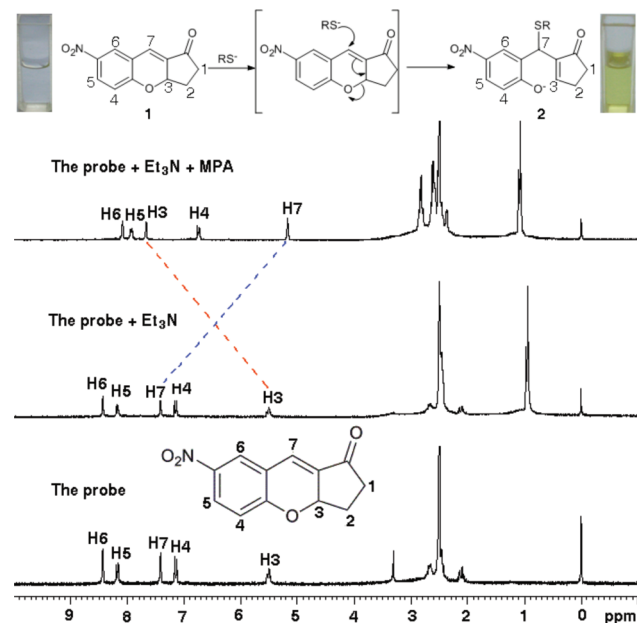
Under the same conditions, probe **1** exhibits a similar response to other thiol-containing compounds such as Hcy and GSH (Figure S5, Supporting Information). The time-dependent reaction of probe **1** for Hcy and GSH gave observed rate constants at pH 7.0 and  $25\ ^\circ\text{C}$  of  $k_{\text{obs}} = 0.065\ \text{s}^{-1}$  with  $t_{1/2} = 10.7\ \text{s}$  for Hcy and  $k_{\text{obs}} = 0.082\ \text{s}^{-1}$  with  $t_{1/2} = 8.5\ \text{s}$  for GSH (Figures S6 and S7, Supporting Information).

It was found during experiments that the new maximum absorption appeared at 405 nm (assigned to that of nitrophenolate, which is often used as a product in enzyme model cleavage experiments<sup>17</sup>) and we speculate that this may be a result of the release of the 4-nitrophenolate group (Scheme 2) through chromene ring-opening, based on a nucleophilic attack on the sulfhydryl group by probe **1** (Michael addition).<sup>11c,13a,15c,d,e</sup> The excision of the 4-nitrophenolate group should be responsible for the yellow color change. To verify this particular hypothesis, the response to mercaptopropionic acid (MPA) by probe **1** was investigated by 1D  $^1\text{H}$  NMR spectroscopic analysis ( $\text{DMSO}-d_6$ ,  $25\ ^\circ\text{C}$ , TMS as an internal reference) in the absence and presence of MPA (Scheme 2, bottom). With addition of MPA (2 equiv) to probe **1** in  $\text{DMSO}-d_6$ , the signals of the aromatic protons shifted upfield to ( $\delta$  6.75, 7.93, 8.09) from their original resonances ( $\delta$  7.14, 8.18, and 8.43, respectively) due to the electron-rich phenolate oxygen atom. The resonance of the original chiral proton (H3) at 5.51 ppm disappeared and a

(17) (a) Wu, C. S.; Wu, C. T.; Yang, Y. S.; Ko, F. H. *Chem. Commun.* **2008**, 5327–5329. (b) Humphry, T.; Forconi, M.; Williams, N. H.; Hengge, A. C. *J. Am. Chem. Soc.* **2002**, *124*, 14860–14865. (c) Rawlingsa, J.; Cleland, W. W.; Hengge, A. C. *J. Inorg. Biochem.* **2003**, *93*, 61–65.

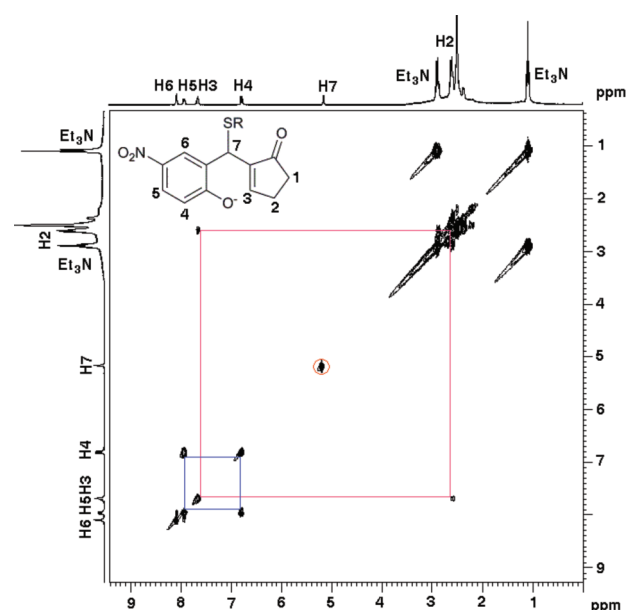


**Scheme 2.** (Top) The Proposed Detection Mechanism for Probe **1** and (Bottom)  $^1\text{H}$  NMR Spectral Change of the Probe **1** (1 mM) upon Addition of MPA (2 mM) in the Presence of  $\text{Et}_3\text{N}$  in  $\text{DMSO}-d_6$



peak at 7.67 ppm ( $=\text{CH}_{\text{cyclopent-2-enone}}$ ) appeared. The signal of the chromene proton H7 changed to 5.18 ppm (assigned as a chiral proton) from the original 7.41 ppm. These implied the formation of the new proposed compound **2** as described in Scheme 2 by reacting MPA with **1**. The 2D COSY of **2** correlation experiments provided direct evidence for the above statement and proposed mechanism. As shown in Figure 4, the COSY spectrum of **2** exhibits clear cross-peaks between H3 ( $=\text{CH}_{\text{cyclopent-2-enone}}$ ) and H2 (the alkyl protons) indicated by a red square, with the blue square showing the interrelation of H4 and H5. The proton H7 (red circle) was isolated and did not relate to any other protons.

In summary, the current study has successfully developed a new, highly sensitive and selective thiol-reactive colorimetric probe, using a chromene molecule for the first time on the basis of a novel mechanism in low micromolar level in an aqueous environment. The probe is easy to prepare via the Baylis–Hillman reaction and intramolecular Michael addition in the presence of imidazole. The whole recognition process brought evident color changes from colorless to



**Figure 4.** 2D  $^1\text{H}$ – $^1\text{H}$  COSY (300 MHz) correlation experiment of the proposed compound **2** in  $\text{DMSO}-d_6$ .

yellow that are clearly visible to the naked eye. This is perhaps a model for developing new colorimetric or fluorescent thiol probes, based on a number of chromene derivatives.<sup>18</sup> We believe this approach could be extended to many more receptors and may result in a new generation of optical sensors due to its merits, according to Zacharis.<sup>14b</sup> Further thiol probe designs are actively being researched in our laboratory.

**Acknowledgment.** The work was supported by the National Natural Science Foundation of China (No.20801032), the Shanxi Province Science Foundation for Youths (No.2009021006-2), and the Shanxi Province Foundation for Returnees (No. 200815).

**Supporting Information Available:** Detailed experimental procedures,  $^1\text{H}$ ,  $^{13}\text{C}$  NMR, and full UV–visible spectra, kinetic study, and crystal data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL901951H

(18) (a) Lee, K. Y.; Kim, J. M.; Kim, J. N. *Bull. Korean Chem. Soc.* **2003**, *24*, 17–18. (b) Ramachary, D. B.; Reddy, Y. V.; Kishor, M. *Org. Biomol. Chem.* **2008**, *6*, 4188–4197.