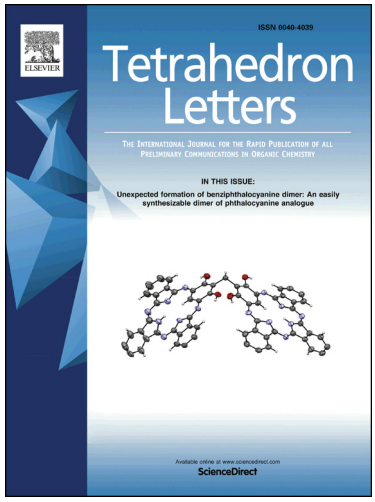


Selective Synthesis of 2-Aminobenzoxazoles and 2-Mercaptobenzoxazoles by Using *o*-Aminophenols as Starting Material

Min Liu, Meng-Tian Zeng, Wan Xu, Li Wu, Zhi-Bing Dong

PII: S0040-4039(17)31252-2
DOI: https://doi.org/10.1016/j.tetlet.2017.09.092
Reference: TETL 49362

To appear in: *Tetrahedron Letters*

Received Date: 23 August 2017
Revised Date: 25 September 2017
Accepted Date: 29 September 2017

Please cite this article as: Liu, M., Zeng, M-T., Xu, W., Wu, L., Dong, Z-B., Selective Synthesis of 2-Aminobenzoxazoles and 2-Mercaptobenzoxazoles by Using *o*-Aminophenols as Starting Material, *Tetrahedron Letters* (2017), doi: https://doi.org/10.1016/j.tetlet.2017.09.092

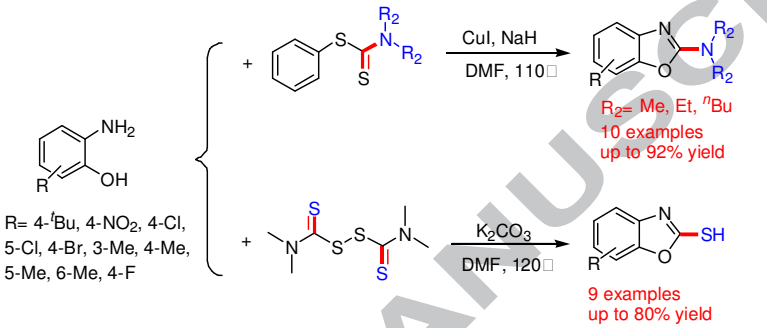
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Selective Synthesis of 2-Aminobenzoxazoles and 2-Mercaptobenzoxazoles by Using *o*-Aminophenols as Starting Material

Min Liu [a], Meng-Tian Zeng [a], Wan Xu [a], Li Wu [a], Zhi-Bing Dong [* a, b]

[a] *School of Chemistry and Environmental Engineering, Wuhan Institute of Technology, Wuhan 430205, P. R. China*
[b] *Key Laboratory of Green Chemical Process, Ministry of Education, Wuhan Institute of Technology, Wuhan 430205, P. R. China*



Tetrahedron Letters
journal homepage: www.elsevier.com

Selective Synthesis of 2-Aminobenzoxazoles and 2-Mercaptobenzoxazoles by Using *o*-Aminophenols as Starting Material

Min Liu[a], Meng-Tian Zeng[a], Wan Xu[a], Li Wu[a], Zhi-Bing Dong[* a, b]

Dedicated to Prof. Herbert Mayr at Ludwig-Maximilians Universität on the occasion of his 70th birthday

[a] *School of Chemistry and Environmental Engineering, Wuhan Institute of Technology, Wuhan 430205, P. R. China*
[b] *Key Laboratory of Green Chemical Process, Ministry of Education, Wuhan Institute of Technology, Wuhan 430205, P. R. China*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
2-aminobenzoxazoles
2-mercaptobenzoxazoles
o-aminophenols
selective synthesis
base

ABSTRACT

2-Aminobenzoxazoles and 2-mercaptobenzoxazoles were selectively synthesized by treating *o*-aminophenols with dithiocarbamates and tetramethylthiuram disulfide (TMTD), respectively. With the promotion of NaH/CuI, the reaction of *o*-aminophenols with dithiocarbamates gave 2-aminobenzoxazoles with good yield (70-92%) in one pot manner, and 2-mercaptobenzoxazoles were synthesized (yield: 55-80%) in the presence of K_2CO_3 by treating *o*-aminophenols with tetramethylthiuram disulfide (TMTD). The feature of this method includes good to excellent yield, easy performance and broad substrate scope, which makes the protocol practical and attractive in the preparation of some potential pharmaceutically active compounds.

* Corresponding author. Tel.: +86-13554158395; fax: +86-02787195680; e-mail: dzb04982@wit.edu.cn

1. Introduction

Benzoxazole derivatives have attracted medical scientists' interest due to their potential biological activities. Benzoxazole derivatives are used in various drugs and pesticides including various proteases inhibitors, such as chymase inhibitors[1], HIV-1 protease inhibitors[2-3], kinase inhibitors[4-5], receptor agonist[6-7], diacylglycerol acyltransferase I inhibitors[8], butyrylcholinesterase inhibitors[9-10], topoisomerase II inhibitors[11], and cyanine tau aggregation inhibitors[12] (**Figure 1**). In addition, they can be also used as potential positron emission tomography probes for imaging of plaques in Alzheimer's disease[13]. Except the medical science, benzoxazole derivatives could be also applied in the field of materials. They could be used as dopants in the fabrication of bright-blue organic light-emitting diodes to enhance the efficiency and stability due to their fluorescence properties[14-15].

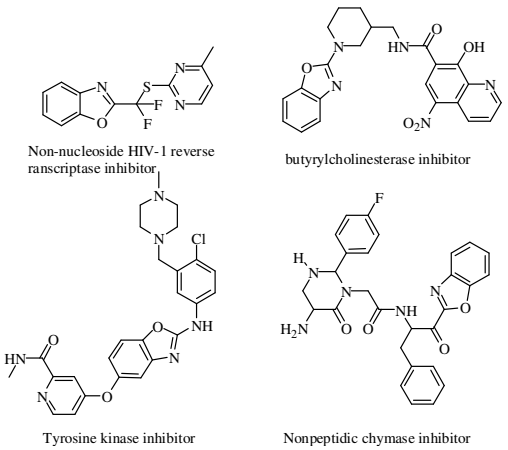
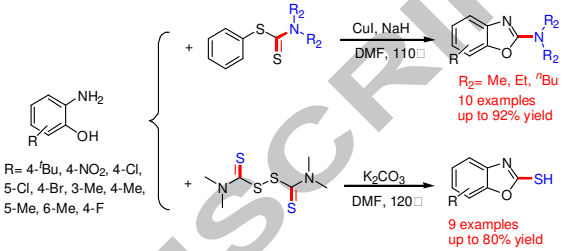


Figure 1. Benzoxazole derivatives with biological activities.

Mercaptobenzoxazoles with essential free thiol group exhibit the expression of potential inhibitory properties. What have been reported are inhibition of human liver iodothyronine 5'-deiodinase[16], tyrosinase inhibition for melanoma targeting[17], inhibitors of alkaline nuclease[18] and antifungal activity[19]. Mercaptobenzoxazoles not only themselves but also the modified nanoparticles and the metal complexes all show biological activities. Haick developed a device called "SNIFFPHONE" that use gold nanoparticles functioned with 2-mercaptobenzoxazole to diagnose lung cancer[20-21]. Co(Ⅱ) and Ru(Ⅱ) complexes with 2-mercaptobenzoxazoles show good antifungal and anticancer activities[22-23].

Various procedures for the synthesis of 2-aminobenzoxazoles were reported, such as 2-substituted benzoxazoles reacting with amine[24], cyclodesulfurization of 2-hydroxyarylthioureas[25] and direct amination of benzoxazoles[26-27]. More importantly, 2-aminobenzoxazoles can be expediently synthesized from 2-aminophenol with chloroformamidinium salts *via* cyclization of guanidine intermediate[28-30]. To the best of our knowledge, the most widely used method to prepare 2-mercaptobenzoxazoles is by treating 2-aminophenols with CS_2 in the presence of KOH[31-34], and 2-mercaptobenzoxazoles could be subsequently transformed to 2-aminobenzoxazoles[31-34]. Both 2-aminobenzoxazoles and 2-mercaptobenzoxazoles can be synthesized starting from 2-aminophenols with aryl isothiocyanates under various conditions[7, 35-37]. While these protocols have some disadvantages, such as toxicity of reactants and catalysts, isolation of intermediates which make them less attractive from a sustainable point of view.

In this work (**Scheme 1**), 2-aminobenzoxazoles and 2-mercaptobenzoxazoles were selectively synthesized by 2-aminophenols reacting with dithiocarbamates and tetramethylthiuram disulfide (TMTD), respectively. With the mediation of CuI, *o*-aminophenols reacted with dithiocarbamates to give 2-aminobenzoxazoles up to 92% yield in one pot manner. 2-Mercaptobenzoxazoles were synthesized up to 80% yield in the presence of K_2CO_3 by treating *o*-aminophenols with tetramethylthiuram disulfide (TMTD).

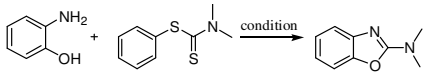


Scheme 1. This work: selective synthesis of 2-aminobenzoxazoles and 2-mercaptobenzoxazoles by using *o*-aminophenols as starting material.

2. Results and Discussion

Initially, we used 2-aminophenol (**1a**) and dithiocarbamate (**2a**) as starting materials to furnish 2-aminobenzoxazole, and the reaction conditions were optimized. Among different solvents, DMF was found to be the most suitable solvent (**Table 1**. **Entry 5**). In order to observe the effect of base on the reaction, various organic and inorganic bases such as NaH, *t*-BuOK, Cs_2CO_3, NEt_3 and *t*-BuONa (**Table 1**. **Entries 5, 7-10**) were tested and the reaction could undergo better in the presence of NaH. Then catalysts were screened to improve the yield. It's disappointing that the yield was not improved when CuI was added as catalyst loading (0.1 equiv) (**Table 1**. **Entry 15**), other catalysts (**Table 1**. **Entries 11-14**) could not help the reaction. Gratifyingly, the reaction underwent well when the loading of CuI and the reaction temperature increased both (**Table 1**. **Entries 17-26**), the optimal copper loading is 1.5 equiv and the best reaction temperature is 110 °C. The optimized reaction conditions were summarized in **Entry 25.**

Table 1. Screening reaction conditions for 2-aminophenol (**1a**) with dithiocarbamate (**2a**)[a]



1a **2a** **3a**

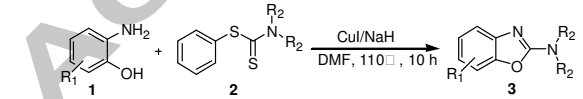
Entry	Catalyst (equiv)	Base (equiv)	Solvent	T (°C)	Yied[b] (%)
1	-	NaH(1.0)	DMSO	60	N.D.[c]
2	-	NaH(1.0)	MeCN	60	N.R.[d]
3	-	NaH(1.0)	DMAC	60	29
4	-	NaH (1.0)	DMF	60	30
5	-	NaH (2.0)	DMF	60	43
6	-	NaH (3.0)	DMF	60	39
7	-	*t*-BuOK (2.0)	DMF	60	33

8		Cs_2CO_3 (2.0)	DMF	60	28
9	-	NEt_3 (2.0)	DMF	60	N.R.[d]
10	-	*t*-BuONa (2.0)	DMF	60	17
11	CuO(0.1)	NaH (2.0)	DMF	60	32
12	$FeBr_3$(0.1)	NaH (2.0)	DMF	60	20
13	$PdCl_2$(0.1)	NaH (2.0)	DMF	60	N.D.[c]
14	$NiCl_2$(0.1)	NaH (2.0)	DMF	60	N.D.[c]
15	CuI(0.1)	NaH (2.0)	DMF	60	36
16	CuI(0.1)	NaH (2.0)	DMF	50	10
17	CuI(0.1)	NaH (2.0)	DMF	80	40
18	CuI(0.1)	NaH (2.0)	DMF	100	45
19	CuI(0.1)	NaH (2.0)	DMF	110	45
20	CuI(0.1)	NaH (2.0)	DMF	120	49
21	CuI(0.2)	NaH (2.0)	DMF	110	47
22	CuI(0.3)	NaH (2.0)	DMF	110	50
23	CuI(0.5)	NaH (2.0)	DMF	110	52
24	CuI(1.0)	NaH (2.0)	DMF	110	55
25	**CuI(1.5)**	**NaH (2.0)**	**DMF**	**110**	**72**
26	CuI(2.0)	NaH (2.0)	DMF	110	74

[a]Reaction conditions: **1a** (1.0 mmol), **2a**(1.2 mmol), solvent (3.0 mL) for 10 h. [b]Isolated yield. [c]N.D.: not determined. [d]N.R.: no reaction.

With the optimal reaction conditions in hand, we began to scope the substrate of 2-aminophenols and dithiocarbamates. Various 2-aminobenzoxazoles (**3a-j**) were synthesized in good yields by reacting 2-aminophenols with dithiocarbamates in the presence of CuI/NaH (**Table 2**). 2-Aminobenzoxazoles bearing the substitutes at the C4 position of hydroxy group were furnished in excellent yields (**Table 2**. **Entries 2-6**, 70-92%). Interestingly, aminophenol substrate with electron withdrawing group such as nitro group at the C4 position resulted in similar high yield with aminophenol bearing electron donating group such as *tert*-butyl group (**Table 2**. **Entries 2**, **3**). Remarkably, 2-aminophenols equipped with methyl group at C3 and C5 position of hydroxyl group gave the products with satisfying yields (**Table 2. Entries 7, 8**). Products bearing 2-(*N,N*-diethylamino) (**3i**) and 2-(*N,N*-dibutylamino) (**3j**) were easily obtained in good yields, showing broad substrate compatibility, which might offer an alternative opportunity for the preparation of 2-aminobenzoxazoles.

Table 2. Substrate scope for tandem reactions of 2-aminophenols with dithiocarbamates [a]



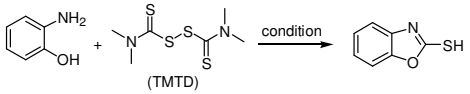
1 2 3

Entry	2-Aminophenols	Dithiocarbamates	Products	Yield[b] (%)
1	1a	2a	3a	75
2	1b	2a	3b	89
3	1c	2a	3c	92
4	1d	2a	3d	70
5	1e	2a	3e	79
6	1f	2a	3f	80
7	1g	2a	3g	78
8	1h	2a	3h	80
9	1a	2b	3i	73
10	1a	2c	3j	85

[a]Reaction conditions: **1** (1.0 mmol), **2** (1.2 mmol), CuI(150 mol%), NaH (2.0 mmol), DMF (3 mL) at 110 °C for 10h. [b]Isolated yield.

Inspired by the reaction between 2-aminophenols with dithiocarbamates and the common block between tetramethylthiuram disulfide (TMTD) and dithiocarbamate, we suspected that the same products might be obtained by 2-aminophenols reacting with tetramethylthiuram disulfide (TMTD). Unexpectedly, an unexpected product named 2-mercaptobenzoxazole was formed in metal-free conditions. Then, the reaction conditions were optimized by screening the bases (**Table 3. Entries 1-9**), base loading (**Table 3**. **Entries 2, 10-12**), solvents (**Table 3. Entries 12-14**) and temperature (**Table 3. Entries 12, 15-18**). The addition of possible catalyst (CuI) did not improve the reaction (**Table 3. Entry 19**). The optimized reaction conditions were summarized in **Entry 18**.

Table 3. Screening reaction conditions for 2-aminophenol (**1a**) with tetramethylthiuram disulfide (TMTD) (**4a**) [a]



1a 4a 5a

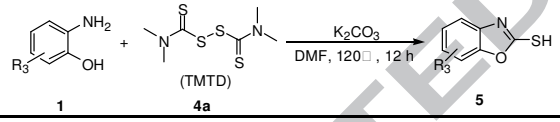
Entry	Base (equiv)	Solvent	T (°C)	Yield[b] (%)
1	KOH(2.0)	DMF	110	24
2	K_2CO_3(2.0)	DMF	110	50
3	*t*-BuOK (2.0)	DMF	110	17
4	NaOH(2.0)	DMF	110	30
5	$NaOCH_3$(2.0)	DMF	110	34
6	Cs_2CO_3(2.0)	DMF	110	14
7	NEt_3(2.0)	DMF	110	14

8	NaO^{t}Bu(2.0)	DMF	110	16
9	NaH(2.0)	DMF	110	32
10	K_2CO_3(0.5)	DMF	110	15
11	K_2CO_3(1.0)	DMF	110	33
12	K_2CO_3(3.0)	DMF	110	66
13	K_2CO_3(3.0)	DMAC	110	52
14	K_2CO_3(3.0)	DMSO	110	45
15	K_2CO_3(3.0)	DMF	60	16
16	K_2CO_3(3.0)	DMF	80	17
17	K_2CO_3(3.0)	DMF	100	34
18	**K_2CO_3(3.0)**	**DMF**	**120**	**80**
19	K_2CO_3(3.0)	DMF	110	54[c]

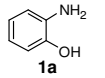
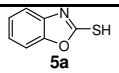
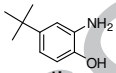
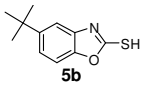
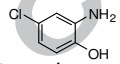
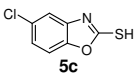
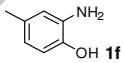
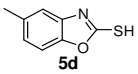
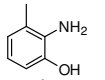
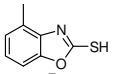
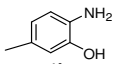
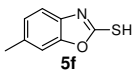
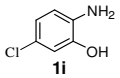
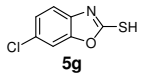
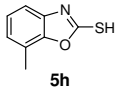
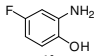
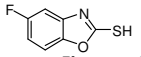
[a]Reaction conditions: **1a** (1 mmol), **4a** (0.6 mmol), solvent (3.0 mL) for 12 h. [b]Isolated yield. [c]catalyzed by CuI (50 mol%).

Under the optimized reaction conditions, the scope of the substrates was investigated as shown in **Table 4**. A number of 2-aminophenols bearing electron donating groups such as *t*-butyl group (**Table 4. Entry 2**) and methyl group (**Table 4. Entry 4-6, 8**) all reacted smoothly to provide the desired products in good yields (70-77%). While products bearing electron withdrawing groups, such as halogen groups (**Table 4. Entry 3, 7, 9**) were obtained in relatively lower yields (55-68%).

Table 4. Substrate scope for tandem reactions of 2-aminophenols with tetramethylthiuram disulfide (TMTD) [a]



1 4a 5

Entry	2-Aminophenols	Tetramethylthiuram Disulfide	Products	Yield[b] (%)
1	 **1a**	TMTD **4a**	 **5a**	80
2	 **1b**	TMTD **4a**	 **5b**	77
3	 **1c**	TMTD **4a**	 **5c**	67
4	 **1f**	TMTD **4a**	 **5d**	72
5	 **1g**	TMTD **4a**	 **5e**	70
6	 **1h**	TMTD **4a**	 **5f**	75
7	 **1i**	TMTD **4a**	 **5g**	68
8	 **1j**	TMTD **4a**	 **5h**	76
9	 **1k**	TMTD **4a**	 **5i**	55

[a]Reaction conditions: **1** (1 mmol), **4a** (0.6 mmol), K_2CO_3 (3.0 mmol), and DMF (3 mL) at 120 °C for 12 h. [b]Isolated yield.

3. Conclusions

In summary, 2-aminobenzoxazoles and 2-mercaptobenzoxazoles were selectively synthesized. With the promotion of NaH/CuI, the reaction of *o*-aminophenols with dithiocarbamates gave 2-aminobenzoxazoles with good yield (70-92%) in one pot manner, and 2-mercaptobenzoxazoles were synthesized (yield: 55-80%) in the presence of K_2CO_3 by treating *o*-aminophenols with tetramethylthiuram disulfide (TMTD). The good to excellent yield, easy performance and broad substrate scope make the protocol practical and attractive in the preparation of some potential pharmaceutically active compounds. The detailed mechanism research and the related application of this protocol are under study in our lab.

4. Experimental Section

General information

^{1}HNMR (in $CDCl_3$ or DMSO-d_6) and ^{13}CNMR (in $CDCl_3$ or DMSO-d_6) spectra were measured using TMS as internal standard on a Bruker 400 AC NMR spectrometer. A high-resolution mass spectra (ESI–HRMS) were determined on an Ion Spec (7.0 T) spectrometer. All starting materials were purchased from commercial suppliers and used without further purification unless otherwise stated. DMSO was dried with molecular sieves. Yields refer to isolated compounds estimated to be 95% pure as determined by ^{1}HNMR and capillary GC analysis.

Typical procedure for the preparation of 2-aminobenzoxazoles in the presence of CuI and NaH (TP_1)

2-Aminophenol (1.0 mmol), NaH (2.0 mmol) was dissolved in DMF (3 mL) in a dried tube, equipped with a magnetic stirring bar and a septum with a balloon. The mixture was stirred for 5 minutes, then dithiocarbamate (1.2 mmol) and CuI (150 mol %) were added. The reaction mixture was then heated at 110 °C and checked by TLC until the starting material was finished (around 10 hours). The reaction was cooled down to room temperature, and quenched with sat. NH_4Cl solution and extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product.

Typical procedure for the preparation of2-mercaptobenzoxazoles in the presence of K_2CO_3 (TP_2)

2-Aminophenol (1.0 mmol), K_2CO_3 (3.0 mmol) was dissolved in DMF (3 mL) in a dried tube, equipped with a magnetic stirring bar and a septum. The mixture was stirred for 5 minutes, and then TMTD (0.6 mmol) was added. The reaction mixture was then heated at 120 °C and checked by TLC until the starting material was finished (around 12 hours). The reaction was cooled down to

room temperature, and then quenched with sat. NH_4Cl solution and extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product.

Acknowledgements

We thank the foundation support from National Natural Science Foundation of China (21302150) Hubei Provincial Department of Education (D20131501), Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry [2012]1707, foundation of Chutian distinguished fellow from Hubei Provincial Department of Education. We thank Prof. Aiwen Lei at Wuhan University (China) for generous NMR analysis support, we also thank Prof. Paul Knochel at Ludwig-Maximilians Universität (Germany) for helpful discussions.

References and note

1. Akahoshi, F.; Ashimori, A.; Sakashita, H.; Yoshimura, T.; Imada, T.; Nakajima, M; Mitsutomi, N.; Kuwahara, S.; Ohtsuka, T; Fukaya, C; Miyazaki, M.; Nakamura, N. *J. Med. Chem.* **2001**, *44*, 1286-1296.
2. Surleraux, D. L. N. G.; A.de Kock, H.; Verschueren, W. G.; Pille, G. M. E.; Maes, L. J. R.; Peeters, A.; Vendeville, S.; Meyer, S. D.; Azijn, H.; Pauwels, R.; de Bethune, M. P.; King, N. M.; Prabu-Jeyabalan, M.; Schiffer, C. A.; Wigerinck, P. B. T. P. *J. Med. Chem.* **2005**, *48*, 1965-1973.
3. Boyer, J.; Arnoult, E.; Médebielle, M.; Guillemont, J.; Unge, J.; Jochmans, D. *J. Med. Chem.* **2011**, *54*, 7974-7985.
4. Potashman, M. H.; Bready, J.; Coxon, A.; DeMelfi, T. M. J. *J. Med. Chem.* **2007**, *50*, 4351-4371.
5. Certal, V.; Halley, F.; Virone-Oddos, A.; Delorme, C. *J. Med. Chem.* **2012**, *55*, 4788-4805.
6. O'Donnell, C. J.; Rogers, B. N.; Bronk, B. S.; Bryce, D. K.; Coe, J. W.; Cook, K. K.; Duplantier, A. J.; Evrard, E.; Hajos, M.; Hoffmann, W. E.; Maklad, R. S.; Hurst. N.; Mather, R. J.; McLean, S.; Nedza, F. M.; T.O'Neill, B.; Peng, L.; Qian, W. M.; Rottas, M. M.; Sands, S. B.; Schmidt, A. W.; Shrikhande, A. V.; Spracklin, D. K.; Wong, D. F.; Zhang, A.; Zhang, L. *J. Med. Chem.* **2010**, *53*, 1222-1237.
7. Mochizuki, M.; Kori, M.; Kobayashi, K.; Yano, T.; Sako, Y.; Tanaka, M.; Kanzaki, N.; Gyorkos, A. C.; Corrette, C. P.; Cho, S. Y.; Pratt, S. A.; Aso, K. *J. Med. Chem.* **2016**, 59, 2551-2566.
8. Zhou, G.; Zorn, N.; Ting, P.; Aslanian, R.; Lin, M. X.; Cook, J.; Lachowicz, J.; Lin, A.; Smith, M.; Hwa, J.; Heek, M. V.; Walker, S. *ACS Med. Chem. Lett*. **2014**, *5*, 544-549.
9. Knez, D.; Brus, B.; Coquelle, N.; Sosič, I.; Šink, R.; Brazzolotto, X.; Mravljak, J.; Colletier, J. P.; Gobec, S. *Bioorg. Med. Chem.* **2015**, *23*, 4442-4452.
10. Matsumura, K.; Ono, M.; Kitada, A.; Watanabe, H.; Yoshimura, M.; Iikuni, S.; Kimura, H.; Okamoto, Y.; Ihara, M.; Saji, H. *J. Med. Chem.* **2015**, *58*, 7241-7257.
11. Li, P. H.; Zeng, P.; Chen, S. B.; Yao, P. F.; Mai, Y. W.; Tan, J. H.; Ou, T. M.; Huang, S. L.; Li, D.; Gu, L. Q.; Huang, Z. S. *J. Med. Chem.* **2016**, *59*, 238-252.
12. Chang, E.; Congdon, E. E.; Honson, N. S.; Duff, K. E.; Kuret, J. *J. Med. Chem.* **2009**, *52*, 3539-3547.
13. Cui, M. C.; Ono, M.; Kimura, H.; Ueda, M. Y.; Saji, H. *J. Med. Chem.* **2012**, *55*, 9136-9145.
14. Ko, C. W.; Tao, Y. T.; Danel, A.; Krzemin´ska, L.; Tomasik, P. *Chem. Mater*. **2001**, *13*, 2441-2446.
15. Shen, Y. J.; Ren, S. W.; Wang, B. K. *J. East China. Inst. Chem. Tech.* **1990**, *16*, 480-488.
16. Harbottle, R.; Richrdson, S. J. *Biochem. J.* **1984**. *217*, 485-491.
17. Mars, U.; Larsson, B. S. *Pigment Cell Res.* **1995**. *8*. 194-201.
18. Bronstein, J. C.; Weber, P. C. *Anal. Biochem.* **2001**. *293*, 239-245.
19. Ramón, G. D.; Ana, C. G.; Carmen, C.; Gerardo, A. F.; Lucas, D. C.; Jorge, G. *Internet Electron. J. Mol. Des*. **2002**, *1*, 339-350.
20. Peng, G.; Tisch, U.; Adams, O.; Hakim, M.; Shehada, N.; Broza, Y. Y.; Billan, S.; Abdah-Bortnyak, R.; Kuten, A.; Haick, H. *Nat. Nanotechnol*. **2009**. *4*. 669-673.
21. Tisch, U.; Schlesinge, I.; Ionescu, R.; Nassar, M.; Axelrod, N.; Robertman, D.; Tessler, Y.; Azar, F.; Marmur, A.; Aharon, P. J.; Haick, H. *Nanomedicine*. **2013**. 8. 43-56.
22. Jain, C.; Nagar. M. G.; Seth, J. *Chem. Pharm. Res*. **2013**, 5. 501-505.
23. Mitra, R.; Samuelson; G. *Eur. J. Inorg. Chem.* **2014**, *2014*, 3536-3546.
24. Benassi, R.; Grandi, R.; Pagnoni, U. M.; Taddei, F.; Bocelli, G.; Sgarabotto, P. *J. Chem. Soc. PERKIN TRANS. II*. **1985**. *4*. 1513-1521.
25. Qian, X. H.; Li, Z. B.; Song, G. H.; Li, Z. *J. Chem. Res*. **2001**, *4*, 138-139.
26. Cho, S. H.; Kim, J. Y.; Lee, S. Y.; Chang, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 9127-9130.
27. Li, Y. M.; Xie, Y. S.; Zhang, R.; Jin, K.; Wang, X. N.; Duan, C. Y. *J. Org. Chem.* **2011**, *76*, 5444-5449.
28. Ohno, K.; Kusakari, W. I.; Kamata, K.; Oda, K.; Machida, M. *Heterocycles*. **2003**, *59*, 317-322.
29. El-Faham, A.; Chebbo, M.; Abdul-Ghani, M.; Younes, G. *J. Heterocyclic Chem*. **2006**, *23*, 599-606.
30. Katari, N. K.; Venkatanarayana, M.; Seinivas, K. *J. Chem. Sci.* **2015**, *127*, 447-453.
31. Venkatachalam, T. K.; Pierens, G. K.; Reutens, D. C. *Lett. Org. Chem.* **2010**, *7*, 519-527.
32. Guntreddi, T.; Allam, B. K.; Singh. K. N. *RSC Adv*, **2013**, *3*, 9875-9880.
33. Yan, S.; Zhang, C.; Wang, Y. H.; Cao, Z.; Zheng, Z.; Hu, X. P. *Tetrahedron Lett*. **2013**, *54*, 3669-3672.
34. Raju, G. N.; Prasanna, T. S. K. T.; Surekha, M. K. L.; Suneetha, M.; Nadendla, R. R. *World J. Pharm. Pharma. Sci*. **2015**, *4*, 1082-1093.
35. Ghosh, H.; Yella, R.; Nath, J.; Patel, B. K. *Eur. J. Org. Chem.* **2008**, *2008*, 6189-6196.
36. Ogura, H.; Mineo, S.; Nakagawak, K. *Chem. Pharm. Bull*. **1981**, *29*, 1518-1524.
37. Jing, Y. F.; Liu, R. T.; Lin, Y. H.; Zhou, X. G. *SciChina Chem.* **2014**, *57*, 1117-1125.

Highlights:

●2-Aminobenzoxazoles are selectively synthesized in good yields in the presence of CuI/NaH.

●2-Mercaptobenzoxazoles are selectively synthesized the presence of K_2CO_3.

●The main difference of the two thio substrates in this work is the S-S block.