# $I_2$-Mediated reaction of amine and benzo[d]oxazole-2(3*H*)-thione in the synthesis of sulfenylated thiazolines

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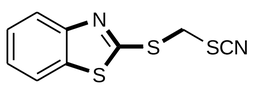
## Abstract

A green and efficient iodine-catalyzed cross-dehydrogenative C–S coupling strategy for the synthesis of benzo[d]thiazolidines was developed. This method enables the direct sulfenylation of benzo[*d*]oxazole-2(3*H*)-thione under mild conditions, providing a cost-effective and sustainable approach in a one-pot synthesis. The reaction's scope and functional group compatibility were explored, leading to benzo[d]oxazole-2-thiol derivatives in moderate to good yields.

## Introduction

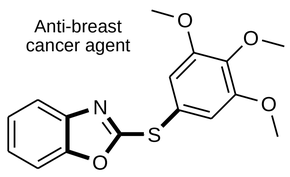
Compound containing C-S bonds have become an indispensable part in many fields, such as organic synthesis, biomedicine, medicinally active molecules[1]. Numerous benzo[d]oxazole-2-thiol derivatives such as [(1,3-benzothiazol-2-yl)sulfanyl]methyl thiocyanate, 2-[(3,4,5-trimethoxyphenyl)sulfanyl]-1,3-benzoxazole and 6-methoxy-2-[(1-phenyl-1H-tetrazol-5-yl)sulfanyl]-1,3-benzothiazole have demonstrated significant value in either agrochemical industry or medicinal chemistry owning to their broad spectrum activities including fungicide, anticancer, and protein phosphatase inhibitor as shown in Figure 1[1].

TCMTB (fungicide)



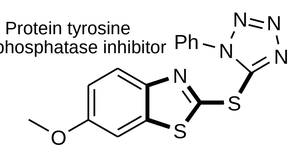
[(1,3-benzothiazol-2-yl)sulfanyl]methyl thiocyanate

Anti-breast cancer agent

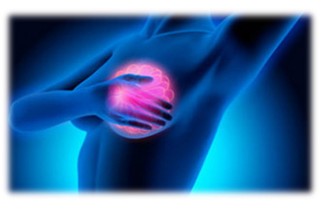


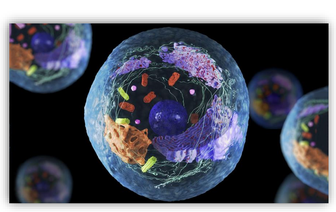
2-[(3,4,5-trimethoxyphenyl)sulfanyl]-1,3-benzoxazole

Protein tyrosine phosphatase inhibitor

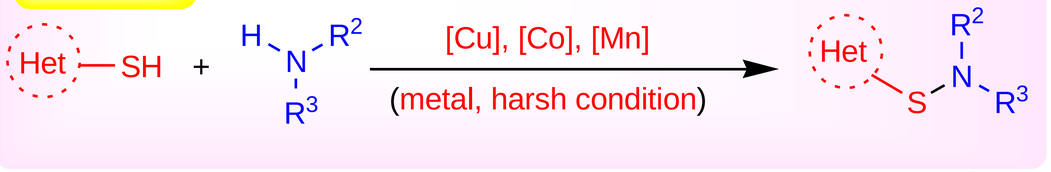


6-methoxy-2-[(1-phenyl-1*H*-tetrazol-5-yl)sulfanyl]-1,3-benzothiazole

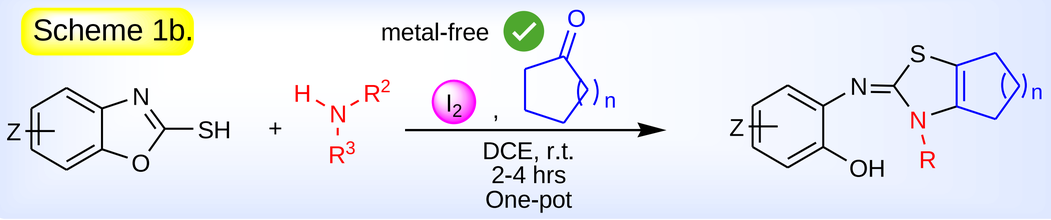




**Scheme 1a**




**Scheme 1b.**




Whereas numerous procedures have been reported for the synthesis of **benzo[d]oxazole-2-thiol** derivatives[2], the available methods remain limited and often require metal catalysts, harsh conditions, and prolonged reaction times (Scheme 1a). The costs associated with removing residual catalysts in metal-catalyzed reactions have prompted us to develop a **metal-free reaction** that employs simple reagents and utilizes **iodine**, an inexpensive and highly abundant reagent, for the sulfenylation process(Scheme 1b).

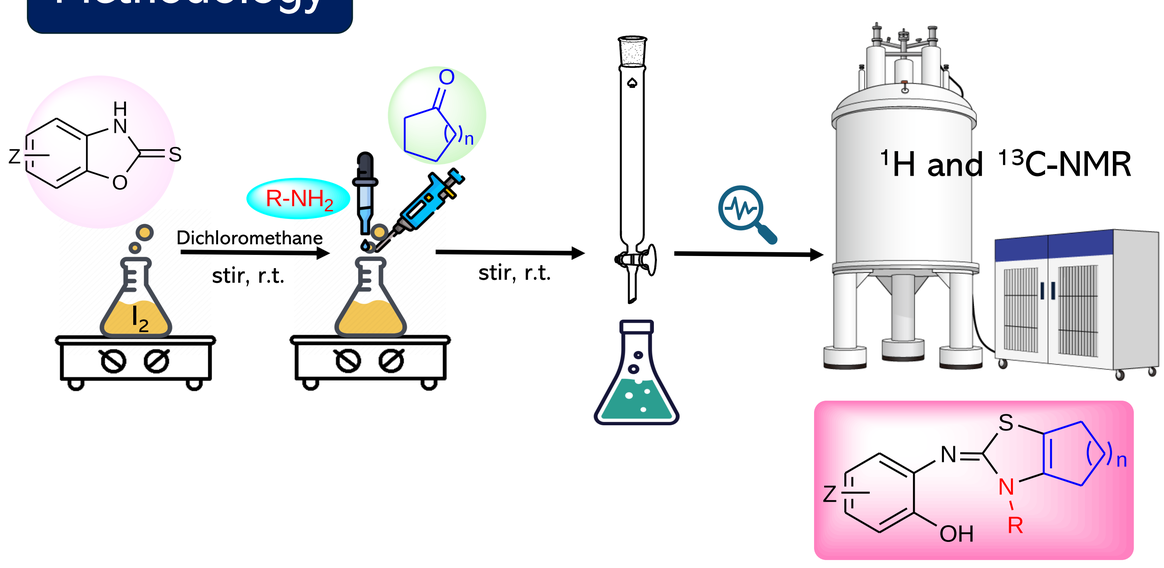
## Objective

1. To study new methods for synthesis of benzo[d]oxazole-2-thiol derivatives
2. To study the effect of the substitution on the structure on the yields

## Conclusions

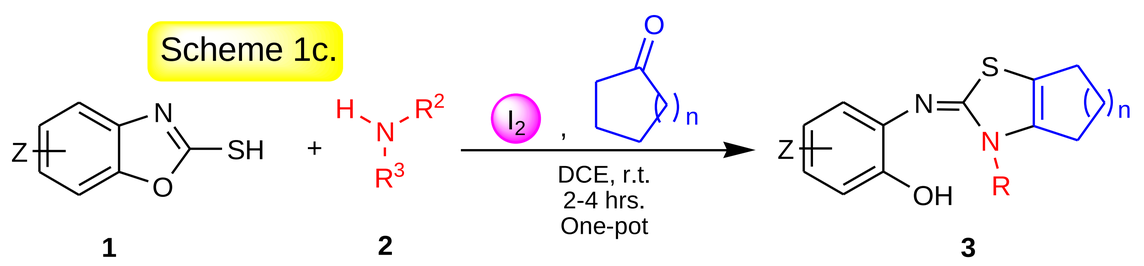
In summary, we have developed a practical method for the synthesis of benzo[d]oxazole-2-thiol derivatives starting from heterocyclic thiols, amine and ketone. By using iodine ($I_2$) as catalyst and oxidant, various thiols, amines (mainly 1° amines) and ketone (mainly cyclic ketones) the synthesis of the target product with good yields and shown metal-free, short reaction time, easy performance, showing potential for the preparation of diversity of biological pharmaceutical active compounds.

## Methodology

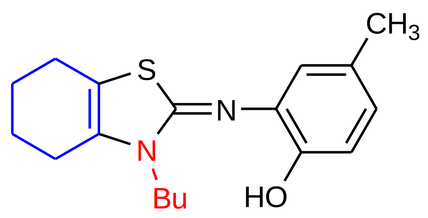



## Results and Discussion

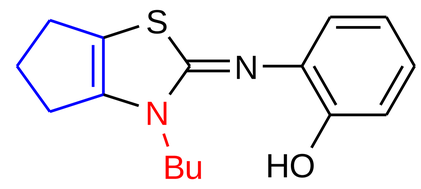
**Scheme 1c.**



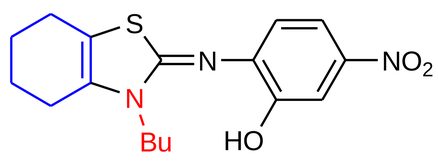

For our study, we chose benzo[d]oxazole-2-thiol (**1**) as a starting material for the synthesis of benzo[d]oxazole-2-thiol derivatives as shown in Scheme 1c.



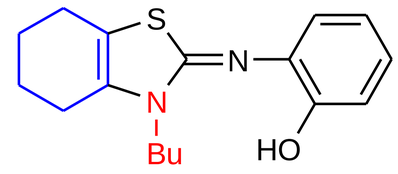
3a (82%)



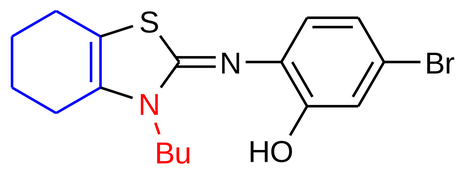
3b (37%)



3c (99%)



3d (Trace)



3e (Trace)

To our delight, aryl thiols (**1**) which have electron-donating or withdrawing groups could be converted to the desired sulfides in good to excellent yields.

## References

1) Yogesh Siddaraju, Kandikere Ramaiah Prabhu. *J. Org. Chem.* **2016**, *81*, 7838-7846.
2) S. H. Ryu, J. Ra, H. M. Ko, *Asian J. Org. Chem.* **2020**, *9*, 933–938.