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# Highly efficient synthesis of 2-mercaptobenzothiazole derivatives in water: metal sulfide-disulfide dynamic interchange reaction

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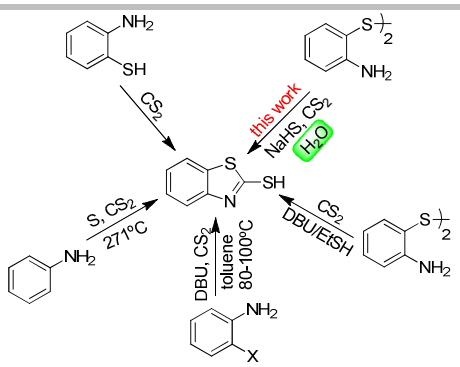
A convenient and efficient method for the synthesis of 2-mercaptobenzothiazoles from disulfide and $CS_2$ mediated by metal sulfide in water is described. This synthetic methodology could be used to prepare diverse 2-mercaptobenzothiazole derivatives in good to excellent yields. In this paper, the concept of metal sulfide-disulfide dynamic interchange reaction was put forward. Then the intermediates of the interchange reaction between NaHS and disulfde were detedted by LC-MS, which demonstrated the S-S bond of disulfide could be broken by metal sulfide through the dynamic interchange reaction. In addition, NaHS was eventually transformed into the sulfur $S_8$ by the dynamic interchange reaction. Moreover, the underlying mechanism of 2-mercaptobenzothiazole formation is proposed, in which NaHS not only acts as the S-S bond cleaving agent but also as an activator of $CS_2$. As a result, a novel synthetic route for the preparation of sulfur-containing heterocycles from disulfide is developed.

## Introduction

2-Mercaptobenzothiazole and its derivatives (MBTs) are an important class of heterocyclic compounds. In bioactive properties,[1] the MBTs are often used to prepare antimicrobial, anti-inflammatory, anthelmintic and anti-tubercular drugs. In industrial applications,[2] MBTs are used as an accelerator in rubber vulcanization[3] and regarded as the promising ligands for the metallic complexes that can be used as luminescent materials.[4] Thus, the study of synthetic methods for preparing MBTs continues to be one of the most attractive areas in synthetic chemistry.[2]




**Scheme 1** Synthesis of 2-mercaptobenzothiazole from $CS_2$

The MBTs prepared through the reactions of carbon disulfide with aniline,[5] o-haloaniline,[6] o-aminothiophenols[7] or disulfide[8] have been widely reported (Scheme 1). However, each suffers from various inherent drawbacks such as long reaction time, high temperature, expensive and toxic solvent. Notably, although the o-aminothiophenol was often used as raw materials to prepare MBTs, most o-aminothiophenols containing various substituted groups could not be prepared easily and often spontaneously formed the corresponding disulfides.[9] Hence, an efficient method for synthesizing MBTs from disulfide under mild condition is still highly desirable.

Disulfide is an important starting material and intermediate for preparing sulfur-containing compounds.[10] To utilize disulfides as starting materials for the MBTs, the cleavage of S-S bond is a key step in the construction of C-S bond. So far, the sulfur-sulfur bond could be cleaved by nucleophilic,[11] free radical reagents[10a, 10e] and metal catalysts.[12] However, due to the inherent stability and kinetic inertness of disulfide, the cleavage of S-S bond under mild conditions, especially in water, is difficult.

Fortunately, thiol-disulfide dynamic interchange reaction was widely used to cleave disulfide in water in biochemistry.[13] In addition, thiol-disulfide dynamic interchange reaction has also been used to break disulfide bond to prepare sulfur-containing heterocylcles in our previous work.[8a] However, the thiol-disulfide dynamic interchange reaction requires high cost organic base and thiols which have unpleasant smell. Furthermore, this reaction also produces another disulfide byproduct. To overcome this drawback, Teppema[8b] has explored the method for the preparation of 2-mercaptobenzothiozole from the reaction of 2,2'-disulfanediyldianiline with $CS_2$ in the presence of metal sulfide in 1927. However, Teppema's work did not show how the

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† Electronic Supplementary Information (ESI) available: The detailed mechanism, LC-MS spectrometry, Crystallographic details of $S_8$, NMR spectra. See DOI: 10.1039/x0xx00000x

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metal sulfide broke S-S bond. Recently, our group had reported that sodium sulfide ($Na_2S$) could cleave the disulfide bond in the synthesis of 2-aryl substituted benzothiazoles.[14] Nevertheless, the underlying mechanism of cleaving S-S bond by metal sulfide is still unclear. Accordingly, exploring the reaction mechanism of S-S bond cleavage is an important research interest.

Herein, we envisioned the low-cost inorganic metal sulfide could be used to replace organic thiols to render the metal sulfide-disulfide dynamic interchange reaction. Therefore, the preparation of MBTs is used as a model reaction to explore the application of the dynamic interchange reaction between metal sulfide and disulfide. Furthermore, the profound function of metal sulfide in this reaction system has also been investigated. To the best of our knowledge, it was the first time to put forward and substantiate the mechanism of the metal sulfide-disulfide dynamic interchange reaction, which demonstrated how the S-S bond of disulfide was cleaved by metal sulfide. As a result, the new mechanism of breaking disulfide seems to provide a novel synthetic route for preparing the sulfur heterocycles from disulfide.

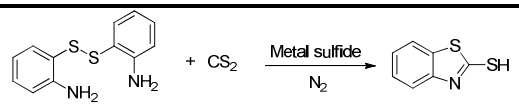
## Results and discussion

The metal sulfide was explored as a catalyst for the synthesis of 2-mercaptobenzothiazole from the reaction of disulfide and $CS_2$. As indicated in Table 1, various parameters such as different metal sulfides, temperature, solvent and the ratio of disulfide to metal sulfide were screened to achieve the optimal reaction conditions. Initially, various temperatures were tested to carry out the reaction of 2,2'-disulfanediyldianiline (**1a**) and $CS_2$ mediated by sodium sulfide nonahydrate under inert atmosphere in water. The highest yield of the desired product **2a** was achieved at 80 °C (Entries 1-4). When sodium hydrosulfide was used to replace the sodium sulfide nonahydrate in this reaction, the yield of product **2a** was slightly increased (Entries 2 and 6). However, when metal sulfide was not used in this reaction, product **2a** was obtained in only 39 % yield (Entry 7), which demonstrated that metal sulfide was important in this reaction system. Then the influence of various ratios of NaHS on the yield of product **2a** was investigated (Entries 8-10 and 6), which showed that 0.5 equiv. of NaHS was the optimal ratio. Moreover, different solvents were tested in the reaction system. Water was used as environment friendly solvent in the following experiment, although product **2a** could be produced efficiently from the reaction of **1a** with $CS_2$ in ethanol or DMF (Entries 11-12). In addition, the yield of product **2a** decreased when the **1a** reacted with $CS_2$ in air (Entry 5), which may result from the oxidation of intermediate 2-aminobenzenethiol (Scheme 2). Furthermore, to test the efficiency of other metal sufides in this reaction process, we found that $K_2S$ and CaS could also promote the reaction of **1a** and $CS_2$ to form **2a** in excellent yields (Entries 13-14), which indicated all the water soluble metal sulphides could render this reaction smoothly.

After established the optimum conditions (Table 1, entry 6), the scope of the reaction was examined using diversely substituted 2,2'-disulfanediyldianilines to provide the corresponding MBTs, and the results are summarized in Table 2. We observed that the reaction could tolerate many functional groups such as chloro, bromo, fluoro, trifluoromethyl, methylsulfonyl, methoxy and methyl groups (Entries 1-9). As shown, the disulfide bearing electron-withdrawing or electron-donating groups could give the corresponding products **2** in moderate to excellent yields under the optimal reaction conditions. Noteworthy, the electron-donating groups on disulfide could promote the reaction and produce higher yield of the corresponding product. In contrast, the strong electron-withdrawing group substituted disulfide (entry 5) could not react with $CS_2$ in 10 h completely and 35 % starting materials was recovered after the reaction, which further demonstrated that the electron-withdrawing groups impeded the reaction of disulfide with $CS_2$.

Based on the present experimental results and the previously reported thiol-disulfide interchange reaction mechanism,[8a] we proposed a mechanism for NaHS-disulfide dynamic interchange reaction in Scheme 2 (the detailed mechanism is shown in Scheme S1). Firstly, the S-S bond of

**Table 1** Optimization of the reaction conditions[a]




1a 2a

| Entry | Metal sulfide | T(°C) | Ratio[b] | Solvent | Yield (%)[d] |
|---|---|---|---|---|---|
| 1 | $Na_2S·9H_2O$ | 90 | 1:0.5:4 | $H_2O$ | 86 |
| 2 | $Na_2S·9H_2O$ | 80 | 1:0.5:4 | $H_2O$ | 88 |
| 3 | $Na_2S·9H_2O$ | 50 | 1:0.5:4 | $H_2O$ | 75 |
| 4 | $Na_2S·9H_2O$ | 25 | 1:0.5:4 | $H_2O$ | 40 |
| 5[c] | $Na_2S·9H_2O$ | 80 | 1:0.5:4 | $H_2O$ | 77 |
| 6 | NaHS | 80 | 1:0.5:4 | $H_2O$ | 93 |
| 7 | - | 80 | 1:0:4 | $H_2O$ | 39 |
| 8 | NaHS | 80 | 1:1:4 | $H_2O$ | 90 |
| 9 | NaHS | 80 | 1:0.2:4 | $H_2O$ | 73 |
| 10 | NaHS | 80 | 1:0.1:4 | $H_2O$ | 69 |
| 11 | NaHS | 80 | 1:0.5:4 | ethanol | 85 |
| 12 | NaHS | 80 | 1:0.5:4 | DMF | 95 |
| 13 | $K_2S$ | 80 | 1:0.5:4 | $H_2O$ | 82 |
| 14 | CaS | 80 | 1:0.5:4 | $H_2O$ | 91 |

[a]Reaction conditions: **1a** (0.4 mmol), $CS_2$ (1.6 mmol), metal sulfide was added in indicated amount, and solvent (2.5 mL), stirred under $N_2$ atmosphere for 4 h. [b]Ratio is the mole ratio of **1a**: metal sulfide: $CS_2$. [c]No protected by $N_2$. [d]Isolated yield based on **1a** after column chromatography.

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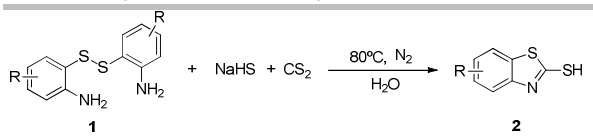
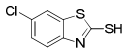
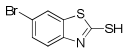
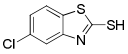
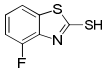
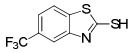
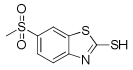
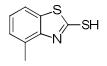
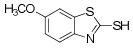
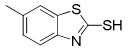
disulfide **1a** is cleaved by the hydrosulfide ion ($HS^-$) through the dynamic interchange reaction, and the intermediates 2-aminobenzenethiolate **B** and persulfide **C** are formed immediately. Simultaneously, the intermediate persulfide **C** continues to react with disulfide **1a** by dynamic interchange reaction to produce the intermediates 2-aminobenzenethiol (**1**) and trisulfide (**2**). The generated intermediate trisulfide (**2**) further reacts with NaHS to afford the persulfide (2-trisulfanylaniline **D**) and **B**. According to this process, the intermediates tetrasulfide (**3**), pentasulfide (**4**), hexasulfide, heptasulfide (**5**), octasulfide and nonasulfide would be produced in this metal sulfide-disulfide interchange reaction process. At last, the persulfide (2-nonasulfanylaniline **E**) could cyclize intramolecularly to form 2-aminobenzenethiol (**1**) and sulfur ($S_8$). All the intermediates reach dynamic equilibrium in the solution. When the electrophilic reagent was added into this solution, the intermediates 2-aminobenzenethiolate **B** and 2-aminobenzenethiol (**1**) would decrease and the dynamic equilibrium was broken. Eventually, the disulfide is totally converted to the corresponding product by the nucleophilic reaction of 2-aminobenzenethiolate **B** or 2-aminobenzenethiol (**1**) with the electrophilic reagent in the presence of NaHS which would be transformed into the elemental sulfur ($S_8$).

To verify the metal sulfide-disulfide interchange reaction mechanism and clarify the special role of sodium hydrosulfide, we investigated the reaction product by mixing disulfide and sodium hydrosulfide in ethanol at room temperature. After stirring for 20 minutes, the reaction products were characterized by high performance liquid chromatography mass spectrometry (LC-MS). As illustrated in Fig. 1 (The original spectrometry is shown in Fig. S1), the reaction of disulfide with sodium hydrosulfide generated a major product 2-aminobenzenethiol (**1**) and a small amount of

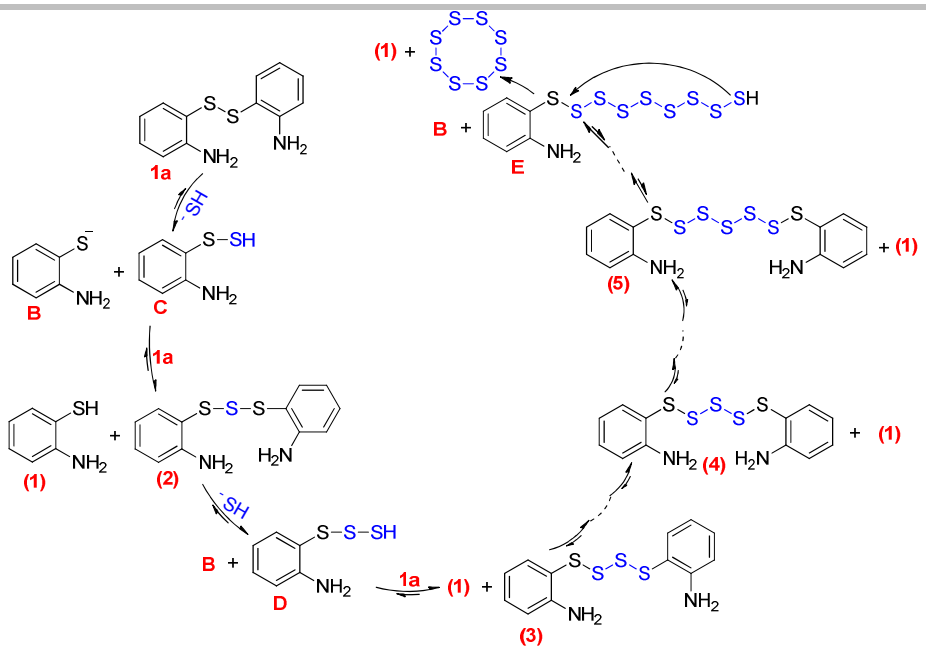
**Table 2** Synthesis of 2-mercaptobenzothiazole derivatives[a]




1 2

| Entry | Substrate **1** | Product **2** | | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | 4,4'-Cl |  | **2b** | 4 | 76 |
| 2 | 4,4'-Br |  | **2c** | 4 | 85 |
| 3 | 3,3'-Cl |  | **2d** | 10 | 63 |
| 4 | 2,2'-F |  | **2e** | 10 | 65 |
| 5 | 3,3'-$CF_3$ |  | **2f** | 10 | 50 |
| 6 | 4,4'-$SO_2CH_3$ |  | **2g** | 8 | 71 |
| 7 | 2,2'-$CH_3$ |  | **2h** | 10 | 86 |
| 8 | 4,4'-$OCH_3$ |  | **2i** | 4 | 90 |
| 9 | 4,4'-$CH_3$ |  | **2j** | 10 | 89 |

[a]Reaction conditions: **1** (0.4 mmol), NaHS (0.2 mmol), $CS_2$ (1.6 mmol) and $H_2O$ (2.5 mL), stirred under $N_2$ atmosphere for 4-10 h. [b]Isolated yield based on substrate **1** after column chromatography.




**Scheme 2** Proposed mechanism of NaHS-disulfide interchange reaction

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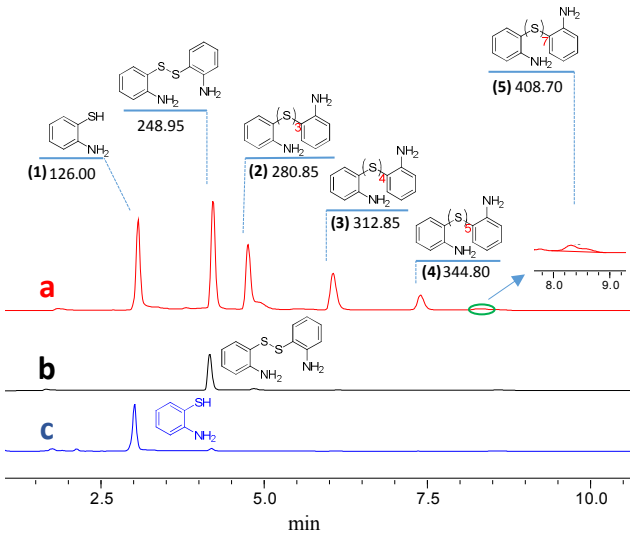
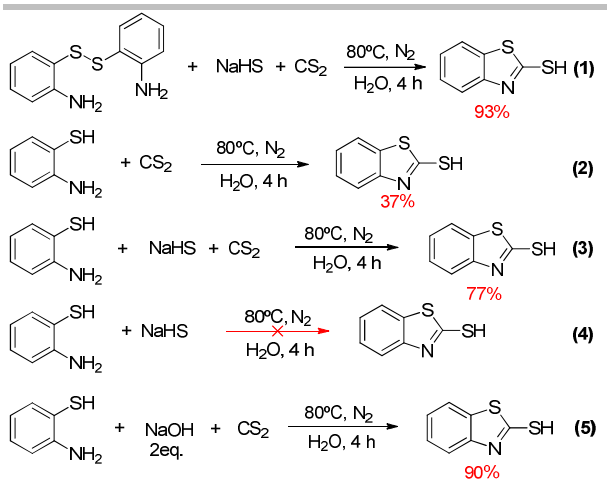



**Fig. 1** (a) LC-MS analysis of the reaction between disulfide **1a** and NaHS after 20 min in ethanol at room temperature (Molecular weight was shown below the molecular structure.), (b) The LC chromatogram of disulfide **1a**, and (c) the LC chromatogram of 2-aminobenzenethiol.

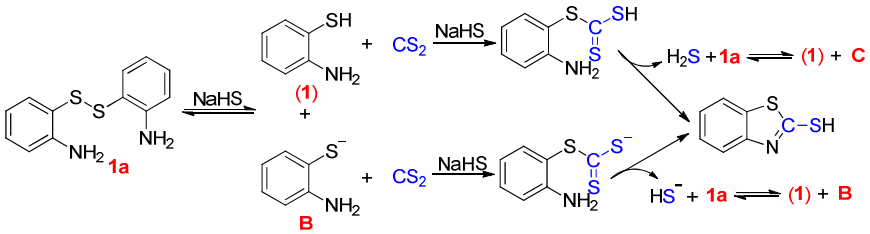
intermediate products such as trisulfide (**2**) and tetrasulfide (**3**), and even smaller amount of pentasulfide (**4**) and heptasulfide (**5**), which demonstrated that the metal sulfide-disulfide interchange reaction could take place easily. These identified intermediates supported our proposed mechanism (Scheme 2). However, persulfide (**C**, **D** and **E**) could not be directly detected by the LC-MS because of their instability.[15]

After the reaction of disulfide **1a** with $CS_2$ catalyzed by NaHS completed, a byproduct was isolated by column chromatography eluted by petroleum ether only. The byproduct was crystalized and analyzed by single crystal X-ray diffraction. The crystal structure (Fig. S2 in SI) indicated the byproduct was the expected sulfur $S_8$, which further confirmed our proposed mechanism of metal sulfide-disulfide interchange reaction.

To shed light on the other functions of NaHS, several controlled experiments were carried out. As shown in Scheme 3, when 2-aminobenzenethiol reacted with carbon disulfide under optimum conditions in the absence of NaHS, product **2a** was formed only in 37 % yield, which demonstrated that NaHS had other roles besides cleaving S-S bond of disulfide (Eqs. 1 and 2). After the addition of NaHS, 2-aminobenzenethiol can be transformed into the desired product **2a** in 77 % yield (Eq. 3). Obviously, 2-aminobenzenethiol cannot react with NaHS to produce **2a** (Eq. 4) and a new peak (236.5 ppm) was presented in the $^{13}$CNMR spectra after mixing the NaHS and $CS_2$ in the deuterated DMF (Fig. S3), which suggested that NaHS could also activate carbon disulfide besides cleaving the disulfide (S-S) bond. However, the yield of **2a** from the reaction of 2-aminobenzenethiol (Eq. 3) was still lower than from the reaction of disulfide (Eq. 1). From the mechanism of NaHS-disulfide interchange reaction (Scheme 2), we found that half




**Scheme 3** Controlled Experiments




**Scheme 4** The proposed mechanism for the reaction of **1a** with $CS_2$ mediated NaHS

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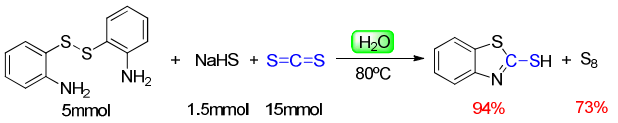


**Scheme 5** A gram-scale reaction of **1a** and $CS_2$[a]
[a]Reaction conditions: 2,2'-disulfanediyldianiline (5.0 mmol, 1.0 equiv.), sodium hydrosulfide (1.5 mmol, 0.3 equiv.), $CS_2$ (15 mmol, 3.0 equiv.), $H_2O$ (25 mL), 80 °C, and stirred in a stainless steel autoclave reactor for 10 h; the yields of product and byproducts ($S_8$) are calculated based on the theoretical amount.

of the disulfide was converted into 2-aminobenzenethiol (**1**) and the other half was transformed into 2-aminobenzenethiolate **B** by NaHS. It is possible that the intermediate 2-aminobenzenethiolate reacted with $CS_2$ more easily than 2-aminobenzenethiol. To verify our idea, the experiment of 2-aminobenzenethiol reacted with $CS_2$ under 2eq. NaOH (Eq. 5) was carried out and the excellent yield of target product was obtained, which demonstrated that 2-aminobenzenethiolate could react with $CS_2$ more easily than 2-aminobenzenethiol.

Based on the S-S bond cleavage process by metal sulfide-disulfide interchange reaction, the reaction mechanism of disulfide and $CS_2$ mediated by NaHS is proposed. Firstly, one equivalent NaHS reacted with one equivalent disulfide to produce one equivalent 2-aminobenzenethiol and one equivalent 2-aminobenzenethiolate **B**. Then 2-aminobenzenethiol and 2-aminobenzenethiolate reacted with $CS_2$ to produce 2-mercaptobenzothiazole by nucleophilic addition and cyclization reaction. Notably, $H_2S$ was formed from the reaction of 2-aminobenzenethiol and $CS_2$, while hydrosulfide ion ($HS^-$) was formed from the reaction of 2-aminobenzenethiolate **B** and $CS_2$. The formed $HS^-$ and $H_2S$ could also cleave S-S bond of disulfide. Therefore, a catalytic amount of NaHS could promote the reaction of disulfide with $CS_2$ smoothly.

To test the reaction's practical utility, a gram-scale reaction was carried out by using 2,2'-disulfanediyldianiline **1a** (5 mmol) under optimum conditions. After the reaction was completed, the crude product was separated by simple filtration. The pure target product and byproduct sulfur ($S_8$) were obtained in excellent yield through column chromatography of the filtrate cake (Scheme 5).

## Conclusions

In summary, we have developed an efficient synthetic method for preparing 2-mercaptobenthiazole derivatives using dynamic interchange reaction between disulfide and metal sulfide in water. Commercially available and easily handled metal sulfide and water were used in this synthetic route. Moreover, the NaHS-disulfide dynamic interchange reaction has firstly been demonstrated and the role of NaHS in activating $CS_2$ has also been proposed in this model reaction.

## Experimental section

### General Procedures

All reagents were used without further purification, which were purchased from Aladdin and Alfa. Most of the reactions were performed in a Wattecs parallel reactor. Reactions were monitored by TLC. Column chromatography separations were carried out on silica gel (200-300 mesh). Melting points were measured with SGC X-4 microscopic melting point meter used uncorrected. Molecular weights were determined by mass spectrometry. The $^1H$ and $^{13}C$ NMR spectra were obtained in $CDCl_3$ or DMSO-$d_6$ on an Agilent 500 MHz DD2 spectrometer and referenced to the residual deuterated solvent or TMS. The NMR results were processed using MestReNova software.

### General Procedure for Synthesis of 2-Mercapbenzothiazole Derivatives (2a-2j).

2,2'-Disulfanediyldianiline or its corresponding derivatives (0.4 mmol), metal sulfide (0.2 mmol NaHS, $Na_2S{\cdot}9H_2O$, $K_2S$ or CaS) in $H_2O$ (2.5 mL) were put into a reaction tube of parallel reactor (Wattecs). The reaction mixture was stirred at 80 °C under $N_2$ atmosphere for the indicated time until the starting material was consumed completely as monitored by TLC and LC-MS analysis. The reaction mixture was acidified by dilute hydrochloric acid (3 mol/L) and extracted with $CH_2Cl_2$ or EtOAc. The organic layers were dried over anhydrous $MgSO_4$. After filtering to remove the $MgSO_4$, the solvent was removed under reduced pressure. The crude product was purified by column chromatography through a silica-gel column to afford the byproduct sulfur $S_8$ eluted by petroleum ether and the desired products eluted by $CH_2Cl_2$ or EtOAc.

### The Reaction Process of 2,2'-Disulfanediyldianiline and NaHS Detected by LC-MS

2,2'-Disulfanediyldianiline (0.2 mmol), NaHS (0.4 mmol) in $CH_3CH_2OH$ (2.5 mL) were put into a reaction tube of parallel reactor (Wattecs). The reaction mixture was stirred at room temperature for 20 min and analyzed by LC-MS. The LC-MS results are shown in Fig. 1 and Fig. S1.

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**The Reaction Procedure of 2-Aminobenzenethiol and $CS_2$**

2-Aminobenzenethiol (1 mmol), $CS_2$ (1.2 mmol), in the presence or absence of NaHS (0.25 mmol) in $H_2O$ (2.5 mL) were put into a stainless steel autoclave reactor. The reaction mixture was stirred at 80 °C for 4 hours. The reaction mixture was acidified by dilute hydrochloric acid (3 mol/L) and extracted with $CH_2Cl_2$ or EtOAc. The organic layers were dried over anhydrous $MgSO_4$. After filtering to remove $MgSO_4$, the solvent was removed under reduced pressure. The crude product was purified by column chromatography through a silica-gel column to afford the desired products in 37.4 % yield (63 mg) in the absence of NaHS or 77 % yield (129 mg) in the presence of NaHS (0.25 mmol) eluted by $CH_2Cl_2$.

**The Reaction Procedure of 2-Aminobenzenethiol and $CS_2$ in the presence of NaOH**

2-Aminobenzenethiol (1 mmol), $CS_2$ (1.2 mmol), and NaOH (2 mmol) in $H_2O$ (2.5 mL) were put into a stainless steel autoclave reactor. The reaction mixture was stirred at 80 °C for 4 hours. The reaction mixture was acidified by dilute hydrochloric acid (3 mol/L) and extracted with $CH_2Cl_2$ or EtOAc. The organic layers were dried over anhydrous $MgSO_4$. After filtering to remove $MgSO_4$, the solvent was removed under reduced pressure. The crude product was purified by column chromatography through a silica-gel column to afford the desired products in 90 % yield (151.2 mg) eluted by $CH_2Cl_2$.

**Characterization data for all products**

2-mercaptobenzothiazole **2a**[16]: 2,2'-disulfanediyldianiline was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 124 mg, 93% yield. Mp: 182-183 °C; MS (EI): m/z 167.1 [$C_7H_5NS_2$], calcd. [M] 167.0. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 13.75 (brs, 1H), 7.69 (d, 1H, J = 9.0 Hz), 7.41-7.38 (m, 1H), 7.32-7.27 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 189.69, 141.13, 129.22, 127.03, 124.08, 121.66, 112.30.

6-chlorobenzo[d]thiazole-2-thiol **2b**[17]: 2,2'-disulfanediylbis(4-chloroaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 122 mg, 76% yield. Mp: 239-241 °C; MS (EI): m/z 200.9 [$C_7H_4ClNS_2$], calcd. [M] 201.0. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 13.86 (brs, 1H), 7.86 (d, 1H, J = 2.0 Hz), 7.44 (dd, 1H, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz), 7.28 (d, 1H, J = 8.5 Hz). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 190.05, 140.13, 130.94, 128.47, 127.16, 121.33, 113.38.

6-bromobenzo[d]thiazole-2-thiol **2c**[17]: 2,2'-disulfanediylbis(4-bromoaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 167 mg, 85% yield. Mp: 265-266 °C; MS (EI): m/z 244.9 [$C_7H_4BrNS_2$], calcd. [M] 244.9. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 13.86 (brs, 1H), 7.98 (d, 1H, J = 2.0 Hz), 7.56 (dd, 1H, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz), 7.22 (d, 1H, J = 8.5 Hz). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 189.94, 140.58, 131.39, 129.84, 124.04, 116.21, 113.78.

5-chlorobenzo[d]thiazole-2-thiol **2d**[18]: 6,6'-disulfanediylbis(3-chloroaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 102 mg, 63% yield. Mp: 199-200 °C; MS (EI): m/z 200.9 [$C_7H_4ClNS_2$], calcd. [M] 201.0. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 13.84 (brs, 1H), 7.72 (d, 1H, J = 8.5 Hz), 7.35 (dd, 1H, $J_1$ =8.5 Hz, $J_2$ = 2.0 Hz), 7.28 (d, 1H, J = 2.0 Hz). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 190.80, 142.14, 131.68, 128.15, 123.95, 123.13, 111.84.

4-fluorobenzo[d]thiazole-2-thiol **2e**[18]: 6,6'-disulfanediylbis(2-fluoroaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 96 mg, 65% yield. Mp: 190-192 °C; MS (EI): m/z 184.9 [$C_7H_4FNS_2$], calcd. [M] 185.2. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 14.22 (brs, 1H), 7.53-7.52 (m, 1H), 7.31-7.24 (m, 2H). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 190.60, 146.77 (d, 1C, J = 247.0 Hz), 131.61 (d, 1C, J = 12.0 Hz), 129.49 (d, 1C, J = 60.0 Hz), 124.95 (d, 1C, J = 25.5 Hz), 117.67 (d, 1C, J = 15.0 Hz), 113.11 (d, 1C, J = 66.0 Hz).

5-(trifluoromethyl)benzo[d]thiazole-2-thiol **2f**[16]: 6,6'-disulfanediylbis(3-(trifluoromethyl)aniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 94 mg, 50% yield. Mp: 205-207 °C; MS (EI): m/z 234.9 [$C_8H_4F_3NS_2$], calcd. [M] 235.0. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 14.03 (brs, 1H), 7.95 (d, 1H, J = 8.5 Hz), 7.64-7.63 (m, 1H), 7.49 (d, 1H, J =1.5 Hz). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 190.95, 141.38, 133.99 (d, 1C, J = 1.3 Hz), 127.54 (q, 1C, J = 32.0 Hz), 123.83 (q, 1C, J = 270.0 Hz), 122.94, 120.44 (q, 1C, J = 3.8 Hz), 108.53 (q, 1C, J = 4.0 Hz).

6-(methylsulfonyl)benzo[d]thiazole-2-thiol **2g**[19]: 2,2'-disulfanediylbis(4-(methylsulfonyl)aniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 134 mg, 71% yield. Mp: 243-244 °C; MS (EI): m/z 245.0 [$C_8H_7NO_2S_3$], calcd. [M] 245.3. $_1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 14.12 (brs, 1H), 8.33 (d, 1H, J = 2.0 Hz), 7.92 (dd, 1H, $J_1$ =8.5 Hz, $J_2$ = 2.0 Hz), 7.47 (d, 1H, J = 8.5 Hz), 3.22 (brs, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 192.02, 144.71, 136.13, 130.01, 126.21, 121.36, 112.53, 43.80.

4-methylbenzo[d]thiazole-2-thiol **2h**[20]: 6,6'-disulfanediylbis(2-methylaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 124 mg, 86% yield. Mp: 191-193 °C; MS (EI): m/z 181.1 [$C_8H_7NS_2$], calcd. [M] 181.0. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 13.57 (brs, 1H), 7.51-7.48 (m, 1H), 7.20 (s, 1H), 7.19 (s, 1H), 2.45 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 190.04, 140.12, 128.94, 128.12, 124.06, 122.50, 118.86, 17.44.

6-methoxybenzo[d]thiazole-2-thiol **2i**[1b]: 2,2'-disulfanediylbis(4-methoxyaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$, Yield: 142 mg, 90% yield. Mp: 203-204 °C; MS (EI): m/z 197.0 [$C_8H_7NOS_2$], calcd. [M] 197.0. $^1$H NMR (500 MHz, DMSO-$d_6$, TMS): δ (ppm) 13.61 (brs, 1H), 7.35 (d, 1H, J = 2.5 Hz), 7.22 (d, 1H, J = 9.0 Hz), 6.99 (dd, 1H, $J_1$ = 8.5 Hz, $J_2$ = 2.5 Hz), 3.77 (s, 3H). $^{13}$C NMR (125 MHz, DMSO-$d_6$, TMS): δ (ppm) 188.24, 156.51, 135.08, 130.58, 114.68, 112.95, 105.81, 55.59.

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6-methylbenzo[d]thiazole-2-thiol **2j**[16]: 2,2'-disulfanediylbis(4-methylaniline) was reacted according to the general procedure affording the product as a white solid. Elute by $CH_2Cl_2$: EtOAc= 30:1, Yield: 129 mg, 89% yield. Mp: 179-181 °C; MS (EI): m/z 181.1 [$C_8H_7NS_2$], calcd. [M] 181.0. $^1$H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) 11.76 (brs, 1H), 7.27 (s, 1H), 7.23 (d, 1H, J =8.0 Hz), 7.18-7.16 (m, 1H), 2.40 (brs, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$, TMS): δ (ppm) 190.23, 138.14, 134.90, 130.13, 128.29, 121.36, 111.91, 21.24.

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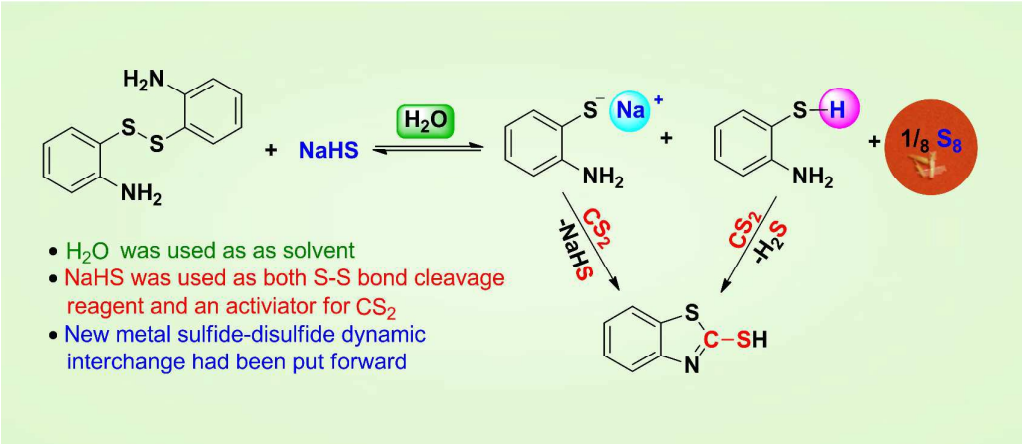


A convenient and efficient method for the synthesis of 2-mercaptobenzothiazoles from disulfide and $CS_2$ was performed by dynamic interchange reaction between disulfide and metal sulfide in water.