

## A CONVENIENT ONE POT SYNTHESIS, CRYSTAL STRUCTURE AND CHEMILUMINESCENCE OF *S,S*-DIPHENYL ETHANEBIS(THIOATE) COMPOUND

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**ABSTRACT.** A compound *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate) is synthesized through one-pot synthesis. The lithiation reaction of 3-bromo-2-methylbenzo[*b*]thiophene by using *n*-butyllithium, is followed by conversion to the corresponding organocopper compound, and subsequent reaction with oxalyl chloride to afford the target compound. The chemical structure of the final compound is well confirmed by NMR, HRMS and X-ray analysis. Meanwhile, the proposed reaction mechanism is fully discussed. Furthermore, the chemiluminescent reaction by using target compound to release light is also investigated. This work provides a convenient synthetic approach for obtaining *S,S*-diphenyl ethanebis(thioate) compound and broadening its application in chemiluminescence.

**KEY WORDS:** One pot synthesis, *S,S*-Diphenyl ethanebis(thioate) compound, Crystal structure, Reaction mechanism, Chemiluminescence

### INTRODUCTION

Diketone and its derivatives are essential intermediate compounds for organic chemistry and coordination chemistry. With the development of the synthesis methods, there are many researchers who use diketone compounds to prepare photochromic diarylethene compounds, such as photoswitchable *N*-heterocyclic carbenes [1-3], threading-gated photochromism in [2]pseudorotaxanes [4], probing aromatic diarylethene photocyclization with light-responsive pyrazine-based systems [5], photochromic diarylethene derivatives having a  $\pi$ -conjugation unit on central aromatic ring [6-9], photochromic diarylethenes with azole unit as ethene bridge [10], and so on.

Meanwhile, the diketone compounds mentioned above can be also utilized for the synthesis of fast photochromic compounds, such as pentaarylbiiimidazole (PABI) [11], phenoxy-imidazolyl radical complex (PIC) [12], and their corresponding negative photochromic compounds [13-15]. Thanks to the superb coordination ability of the double carbonyl groups, the compound containing diketone unit can be also applied for coordination chemistry [16-18].

Along with the intensive study on diketone compounds, their corresponding derivatives have been deep investigated for their deep applications. The chemically-induced geometrical isomerization of the stilbenes during the peroxyoxalate chemiluminescent reactions [19] and chemiluminescence reaction of diaryl oxalate esters oxidized by hydrogen peroxide in the presence of rubrene [20] have been already reported by different research groups. Additionally, another kinds of diketone derivatives *S,S*-diphenyl ethanebis(thioate) compounds have also been widely used in many other application fields. Brinić and coworkers reported that the *S,S'*-bis(2-aminophenyl)-ethanebis(thioate) [21] and its modified analogs [22] can be used as N2S2 donor ligand to improve the response of copper (II) selective PVC membrane electrode. In addition, *S',S''*-diphenyl ethane bis(thioate) and its derivatives can be applied as potent inhibitors of mammalian carboxylesterases (CEs) [23].

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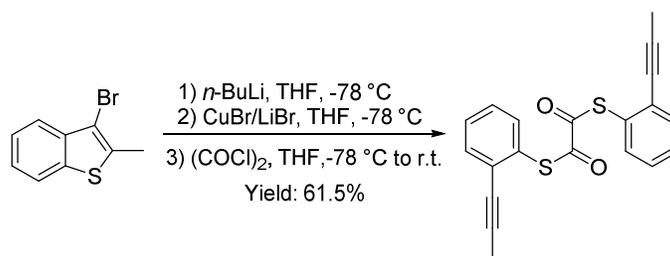
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Even though the applications of the diketone compounds, especially *S*<sup>1</sup>,*S*<sup>2</sup>-diphenyl ethane bis(thioate) compounds, have been extensively studied, the synthetic methods to obtain the target compound are limited [24, 25].

In this study, a convenient one pot synthesis for *S,S*-diphenyl ethanebis(thioate) compound by using benzo[*b*]thiophene as a starting material was reported. The plausible reaction mechanism was well discussed to reveal the reaction process. The final molecular structure was illustrated unambiguously by X-ray crystallographic analysis of the single crystal. Furthermore, the target compound can be also used as chemiluminescent reactions to release light. It is expected that this study will provide important ideas and strategies for the synthesis of *S,S*-diphenyl ethanebis(thioate) compound and broaden its application.

## RESULTS AND DISCUSSION

### Organic synthesis



Scheme 1. Synthetic route of compound *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate).

As depicted in Scheme 1, the target compound *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate) is synthesized by a convenient one pot synthesis. The lithiation reaction of 3-bromo-2-methylbenzo[*b*]thiophene was carried out by using *n*-butyllithium. Then the reaction was followed by conversion to the corresponding organocopper compound, and subsequent nucleophilic reaction with oxalyl chloride to afford the target compound. The details for synthesizing the target compound are in the experimental section.

### Crystal structure

The single crystal of the target compound was successfully obtained from slow evaporation of a hexane/dichloromethane mixture. As shown in Figure 1, the molecular structure of the target compound was unambiguously clarified by X-ray crystallographic analysis. The distance between the ArH6–O atoms in the target compound is 0.2848 nm, which is much larger than the sum of the van der Waals radii of the H (0.12 nm) and O (0.152 nm) atoms. The length between these two atoms indicates no intramolecular hydrogen bonding formation in this molecular. However, the parking modes of the molecules in the crystals suggest that the molecules are aggregated together in a regular manner.

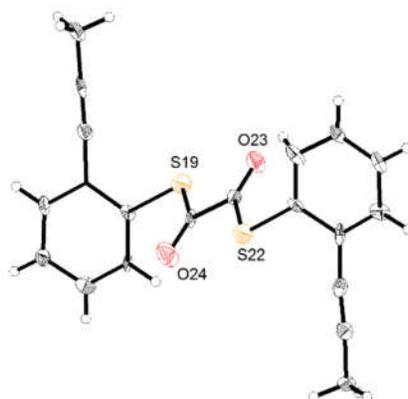


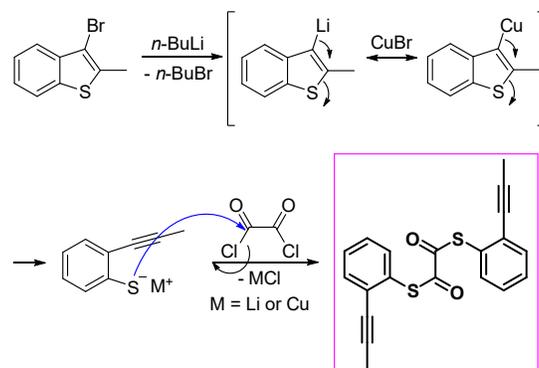
Figure 1. ORTEP representations of the molecular structure of *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate) with thermal ellipsoids (50% probability), where the sulfur atoms are highlighted in yellow and the oxygen atom is highlighted in red.

#### Reaction mechanism

Until now, several references have already been reported for the thiophene ring opening reaction by same groups [26, 27]. However, they just focused on the ring opening reaction by using *n*-butyllithium and no further chemical reaction was investigated. Meanwhile, the chemical reactions described above by using a flow microreactor limited the reaction application adaptability. Similar thiophene ring-opening reaction was also reported in 2020 [28]. Even though the side reaction did not yield diketone compound, it provides a guideline for us to understand the reaction mechanism.

The proposed reaction mechanism for organic synthesis of the target compound is shown in Scheme 2. The lithiation reaction of 3-bromo-2-methylbenzo[*b*]thiophene in position 3 was carried out by using *n*-butyllithium to afford the intermediate organolithium compound. The following conversion reaction with the CuBr forces to form a mixture of corresponding organocopper and organolithium compounds. Then, the cleavage of the thiophene ring can occur at same reaction condition. Finally, the organometal compound can be used as a nucleophile to attack the carbon atom of the oxalyl chloride and finally generate the target yellow compound.

Initially, the CuBr was used for the conversion reaction to get the corresponding organocopper compound and then to inhibit the thiophene ring-opening reaction. However, the organocopper compound could still undergo the ring-opening reaction. At least we can confirm this result from this reaction. From the proposed reaction mechanism investigation, we can also recognize that the thiophene ring will still undergo ring opening reaction after the lithiation reaction with *n*-butyllithium even if the reaction is performed at low reaction temperature (-78 °C). This result not only gives us an insight for the understanding of the thiophene ring opening reaction at low temperature but also provides a new method for the synthesis of *S,S*-diphenyl ethanebis(thioate) compound.



Scheme 2. The proposed reaction mechanism.

### Chemiluminescence

Peroxyoxalate chemiluminescence reaction is always applied to produce energy by the excitation of the fluorescent molecules to emit light [16, 17]. As for the target compound *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate) containing similar unit of peroxyoxalate, we studied the bioimaging application of the target compound for the chemiluminescence reaction in solution. A small bottle was charged with 9,10-diphenyl anthracene as a dye (Figure 2(a)) and target compound *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate). Then the hydrogen peroxide was added to the system, and the bottle exhibited slight blue light color (Figure 2(b)). The plausible reaction mechanism of the chemiluminescence reaction is shown in Figure 2(c), which is similar to the reported reference [16]. This result suggested that the target compound by one pot synthesis could be well used for the chemiluminescence reaction as glow stick or some other applications.

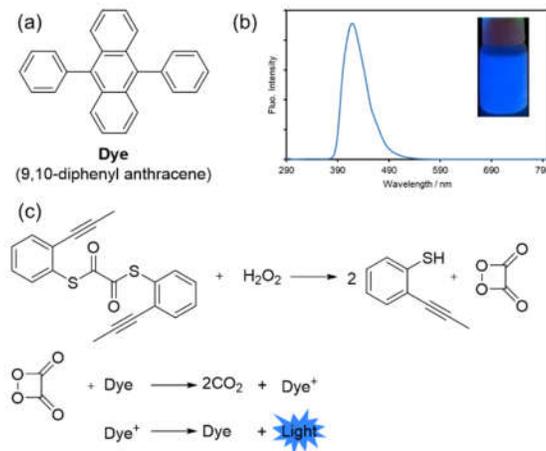


Figure 2. Chemiluminescence of compound *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate). (a) Chemical structure of the dye for chemiluminescent reaction; (b) fluorescence spectrum and chemiluminescent reaction in solution; and (c) the proposed reaction mechanism of the chemiluminescent reaction.

## EXPERIMENTAL

Unless otherwise noted, all reagents and reaction solvents were purchased from Tokyo Chemical Industry Co., Ltd., and were used without further purification. All reaction solvents were distilled on the appropriate drying reagents prior to use. All of the reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254). <sup>1</sup>H NMR spectrum was recorded at 400 MHz on an AVANCE III 400 NanoBay (Bruker). ESI-TOF-MS spectra were recorded on a micrOTOF II-AGA1 (Bruker). The diffraction data of the single crystal were collected on Rigaku XtaLAB mini II with Mo K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) at 100 K. Data integration and reduction were undertaken with Rigaku CrysAlis<sup>Pro</sup>. The data refinement was carried out by Olex<sup>2</sup> software package with SHELXL program.

### *Synthesis procedure*

A solution of *n*-BuLi (1.6 M, 0.62 mL, 0.97 mmol) was added dropwise to a solution of 3-bromo-2-methylbenzo[*b*]thiophene (0.2 g, 0.88 mmol) in anhydrous and degassed THF solution (2 mL) under  $-78 \text{ }^\circ\text{C}$ . The mixture was stirred at this temperature for one hour. Meanwhile, CuBr (126 mg, 0.88 mmol) and LiBr (76 mg, 0.88 mmol) were mixture in anhydrous and degassed THF (5 mL), and the mixture was stirred until a homogenous solution was obtained, and subsequently cooled to  $-78 \text{ }^\circ\text{C}$ . The suspension of 3-lithium-2-methylbenzo[*b*]thiophene was cannula-transferred to the cooled CuBr/LiBr solution, and the mixture was stirred at  $-78 \text{ }^\circ\text{C}$  for one hour. A solution of oxalyl chloride (37  $\mu\text{L}$ , 0.44 mmol) in anhydrous and degassed THF (1 mL) was cooled to  $-78 \text{ }^\circ\text{C}$  and cannula-transferred to the reaction mixture. Then the mixture was stirred overnight at room temperature. The mixture was quenched with 1 M HCl (5 mL), and the organic layer were evaporated under reduced pressure. The crude product was purified by using silica gel chromatography (EtOAc/hexane = 1:4) to get the target compound (0.24 g, 61.5%) as yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.57 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.52 (dd, *J* = 7.6, 1.2 Hz, 2H), 7.42-7.34 (m, 4H), 2.08 (s, 6H). <sup>13</sup>C NMR (100.16 MHz, CDCl<sub>3</sub>):  $\delta$ : 187.0, 132.1, 129.7, 128.3, 125.5, 124.4, 92.1, 80.1, 4.7. HRMS (ESI-TOF) calculated for C<sub>20</sub>H<sub>14</sub>S<sub>2</sub>O<sub>2</sub>Na [M+Na]<sup>+</sup>: 373.0327, found: 373.0327.

## CONCLUSION

In summary, a novel *S,S*-diphenyl ethanebis(thioate) compound, *S,S*-bis(2-(prop-1-yn-1-yl)phenyl) ethanebis(thioate), has been synthesized by a convenient one pot synthesis from 2-methylbenzo[*b*]thiophene. The structure of the final compound was well confirmed by NMR, HRMS and X-ray crystallographic analysis. Meanwhile, the reaction mechanism reveals the reaction process for getting the target compound. This compound has potential application prospects in the field of chemiluminescence and enzyme inhibitors.

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