






## Visible-Light-mediated the Facile Synthesis of Disulfides Using Reusable $\text{TiO}_2/\text{MoS}_2$ Nanocomposite Photocatalyst

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# Visible-light-mediated the facile synthesis of disulfides using reusable TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite photocatalyst

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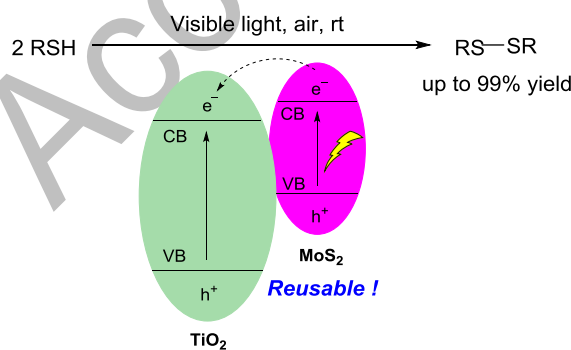
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## Abstract

A nontoxic and inexpensive TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite was prepared and employed as an efficient photocatalyst for the synthesis of symmetrical disulfides under visible light irradiation at room temperature. Both aryl and alkyl thiols survived the reaction conditions, affording the corresponding disulfides in good to excellent yields. The photocatalyst could be easily recovered by simple centrifugation and filtration, and reused several times without significant loss in its activity.

## Graphical Abstract



**KEYWORDS:** Photocatalysis, semiconductor, TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite, disulfides

## 1 Introduction

The direct oxidative coupling of thiols to disulfides is of significant importance in both biological and chemical process.<sup>[1,2]</sup> Various reagents including metal salts<sup>[3-8]</sup> and non-metal oxidating reagents<sup>[9-17]</sup> have been employed for the synthesis of disulfides up to date. However, the toxicity and high cost of some metal salts or non-metal oxidating reagents severely limit their practical use. Recently, much effort in green thiol surrogate,<sup>[18]</sup> green reaction medium<sup>[19]</sup> as well as new reaction technology<sup>[20]</sup> has been realized. However, some drawbacks such as over-oxidation, excess and/or expensive oxidating reagents, high reaction temperatures, long reaction times, and tedious work-up procedures are still issues to be addressed. It should also be pointed out that although thiols are malodorous and air-sensitive, they are commercially available or easily prepared. More importantly, the direct coupling of thiols affords less waste compared with other thiol surrogates.

Oxidation of thiols into disulfide mediated by visible light in the presence of diaryl tellurides,<sup>[21]</sup> iron phthalocyanine immobilized on graphene,<sup>[22]</sup> CdSe quantum dots,<sup>[23]</sup> Eosin Y<sup>[24]</sup> and Rose Bengal<sup>[25]</sup> have also been reported. However, these photocatalysts are either expensive or can not be recovered and reused. We envisioned that an ideal method for synthesis of disulfide would use air or oxygen as a green and cheap oxidant, a

cheap and reusable catalyst to initiate the reaction, and should operate at room temperature without any additives. Recently, semiconductor composites as photocatalysts have received much attention.<sup>[26-29]</sup> Among them, the modified TiO<sub>2</sub> photocatalysts with another semiconductor such as MoS<sub>2</sub> have shown good activities in hydrogen evolution and photo-degradation processes. Moreover, these catalysts are cheap, readily accessible, stable and less-toxic.<sup>[30-33]</sup> Our group also reported a visible-light-induced aerobic thiocyanation of indoles using reusable TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite as the photocatalyst.<sup>[34]</sup> This kind of semiconductor photocatalyst is easily prepared, cheap and effective. Most importantly, it can be easily recycled after reaction by simple centrifugation and filtration. Herein, we wish to report a facile and green procedure for the synthesis of disulfides catalyzed by a recyclable TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite under visible light irradiation at room temperature (Scheme 1).

## 2. RESULTS AND DISCUSSION

The TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite was prepared according to our previous literature<sup>[35]</sup> via a simple hydrothermal process using cheap and readily available TiCl<sub>4</sub>, sodium molybdate and thioacetamide as starting materials. The as-prepared TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite was well characterized by XRD, UV-vis and TEM (See Supplementary Material). With the TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite in hand, 4-chlorothiophenol (**1a**) was selected as the model substrate to explore its photocatalytic activity. The results are summarized in Table 1. No reaction occurred in the presence of either Anatase TiO<sub>2</sub> or Rutile TiO<sub>2</sub>. A 48% yield of

desired product **2a** was obtained in ethanol by using pure MoS<sub>2</sub> as the catalyst (Table 1, entry 3). Further studies clearly showed that TiO<sub>2</sub>/MoS<sub>2</sub> (10: 1, molar ratio of Ti to Mo, 10 mg) was the most effective catalyst, providing **2a** in almost quantitative yield (Table 1, entries 4~8 and 14), indicating that the heterojunction of TiO<sub>2</sub>/MoS<sub>2</sub> is vital for its photoactivity. Reactions in other solvents such as CH<sub>3</sub>CN, DMF, DCM, toluene and water led to decreased yields (Table 1, entries 9~13). Moreover, no desired product was detected in the absence of either light irradiation or TiO<sub>2</sub>/MoS<sub>2</sub>, highlighting the importance of the photocatalytic system. Further studies also revealed that air or oxygen had a pronounced effect on the reaction rate (Table 1, entry 15).

To evaluate the scope and limitations of the current procedure, a series of thiols were tested under the optimized reaction conditions. As shown from Table 2, aryl thiols bearing with either electron-withdrawing or electron-donating substituents such as halide (Cl, Br and F), methyl, methoxy, nitrile group underwent the reaction smoothly to afford the corresponding products in good to excellent yields (85~99%). Sterically hindered thiophenol, such as 2-methoxythiophenol could also be efficiently converted to the corresponding disulfide (**2i**, 85%). The scope of this protocol was further extended to heteroaromatic and aliphatic thiols. As shown from the results, reaction of nitrogen-containing heteroaromatic thiol **1k** and benzylic thiol **1l** proceeded smoothly to deliver the desired products **2k** and **2l** in 97% and 93% yield, respectively. In

comparison, longer reaction time was required for other aliphatic thiols to achieve good yields, which was attributed to the less stability of the alkyl thiol radical intermediates.

To demonstrate the scalability of the present protocol, a gram-scale reaction (10 mmol) was carried out under the optimized conditions (Scheme 2). To our delight, this transformation afforded the desired product **2a** in 87% yield (2.49 g) within 4 h, suggesting a high potential for industry scale-up.

The reusability of the catalytic system is also an advantage of this protocol. After reaction, the catalyst was recovered by centrifugation and filtration, while the product was extracted with ethyl acetate. Using substrate **1a** as example, it was found that the catalytic system could be readily recovered and reused with slight decrease in its activity after eight consecutive runs (99%, 99%, 99%, 96%, 95%, 91%, 90% and 86% yield, respectively). The recovered catalyst was examined by TEM. Aggregation of TiO<sub>2</sub>/MoS<sub>2</sub> was observed and the size of TiO<sub>2</sub>/MoS<sub>2</sub> nanoparticles increased, which might accounted for the decreased activity.

A plausible mechanism is also outlined in Scheme 3 based on the reported literatures.<sup>[33,34]</sup>

Because of the quantum confinement effects of nanoscale MoS<sub>2</sub>, the CB of nanoscale MoS<sub>2</sub> is more positive than that of TiO<sub>2</sub>, thus under visible-light irradiation, the photogenerated electrons from MoS<sub>2</sub> can be transferred into CB of TiO<sub>2</sub>, thereby the

photoinduced electrons and holes are efficiently separated, and the recombination of electron-holes can be reduced. The produced holes oxidize thiol **1** into the corresponding radical cation, which can lose a proton to deliver thiyl radical. Subsequently, homocoupling of thiyl radical affords the disulfide **2**. In another aspect, oxygen acts as a sacrificial electron acceptor, thereby reducing the hole-electron recombination.

### 3. CONCLUSION

In summary, we have developed a facile and environmentally benign photocatalytic method for oxidative coupling of thiols into disulfides using TiO<sub>2</sub>/MoS<sub>2</sub> nanocomposite under visible light. This protocol affords excellent yields, high functional group compatibility, as well as the reusability of the catalyst. Moreover, the reactions are operationally simple and can be performed at room temperature in an open air system without any additives or bases.

### 4. EXPERIMENTAL

#### 4.1. General Remarks

All reagents were obtained from local commercial suppliers and used without further purification. Column chromatography was generally performed on silica gel (300-400 mesh). Thin-layer chromatography (TLC) was visualized using UV light. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker Advance 400 analyzer in Chloroform-d (CDCl<sub>3</sub>) using TMS as an internal standard. Chemical shifts are reported in δ units, parts per

million (ppm). The coupling constants  $J$  are given in Hz. Low-resolution mass spectra was obtained from triple quadrupole GC/MS Agilent technology. High-resolution mass spectrometry (HRMS) was performed on an Agilent 6540 Q-TOF MS instrument with an ESI source. X-ray diffraction (XRD) patterns were collected on a SHIMADZU XRD-6000 diffractometer with Cu Ka radiation at 40 kV and 30 mA. HRTEM (JEM-2010, JEOL) was used to study the microstructures. UV-vis absorption spectra were obtained by a UV-vis spectrophotometer (SOLID 3700, Shimadzu). The specific surface areas were obtained by the Brunauer–Emmett–Teller (BET) method based on nitrogen adsorption/desorption measurements (Micromeritics ASAP 2010C). All the products except **2o** are known compounds and were identified by comparing of their physical and spectra data with those reported in the literature.

#### **4.2. General Procedure For The Synthesis Of Disulfides**

To a solution of thiol **1** (1 mmol) in ethanol (1 mL) was added TiO<sub>2</sub>/MoS<sub>2</sub> (10: 1, molar ratio, 10 mg). The reaction mixture was stirred under a 14 W CFL irradiation at a distance of 10 cm at room temperature for a certain time. After reaction (monitored by TLC), ethyl acetate was added, and the solid catalyst was recovered by centrifugation. The reaction mixture was extracted with ethyl acetate and washed with water. The combined organic phase was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to give the crude residue, which was purified by column chromatography with petroleum ether/ethyl



acetate to afford the pure product **2**. The recovered catalyst was then washed with ethanol and deionized water, dried under vacuum, and reused for the next run.

**1,2-Bis(4-chlorophenyl)disulfane (2a)**: Light yellow solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.39 (d, *J* = 8.5 Hz, 4H), 7.26 (d, *J* = 8.5 Hz, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 129.5, 129.5, 133.8, 135.3; GC-MS: *m/z* 286 [M<sup>+</sup>].

**Dimethyl 2,2'-disulfanediyldiacetate (2o)**: Light yellow solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 3.76 (s, 6H), 3.58 (s, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 169.8, 52.6, 41.1; HRMS (ESI): Calcd. for C<sub>6</sub>H<sub>11</sub>O<sub>4</sub>S<sub>2</sub> (M+H)<sup>+</sup> 211.0093, found 211.0085.

#### ACKNOWLEDGMENTS

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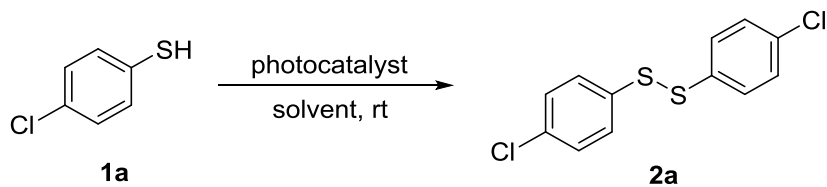
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Table 1. Optimized the reaction conditions<sup>[a]</sup>



Entry	Catalyst	Solvent	Yield(%) <sup>[b]</sup>
1	TiO <sub>2</sub> (Anatase)	EtOH	n.r.
2	TiO <sub>2</sub> (Rutile)	EtOH	n.r.
3	MoS <sub>2</sub>	EtOH	48
4	TiO <sub>2</sub> /MoS <sub>2</sub> (100: 1)	EtOH	53
5	TiO <sub>2</sub> /MoS <sub>2</sub> (50: 1)	EtOH	64
6	TiO <sub>2</sub> /MoS <sub>2</sub> (20: 1)	EtOH	77
7	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	EtOH	>99, n.r. <sup>[c,d]</sup>
8	TiO <sub>2</sub> /MoS <sub>2</sub> (5: 1)	EtOH	94
9	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	CH <sub>3</sub> CN	83
10	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	DMF	71
11	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	DCM	77
12	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	toluene	75
13	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	water	36
14	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	EtOH	68 <sup>[e]</sup> , >99 <sup>[f]</sup>
15	TiO <sub>2</sub> /MoS <sub>2</sub> (10: 1)	EtOH	<5 <sup>[g]</sup> , >99 <sup>[h]</sup>

<sup>[a]</sup> Reaction conditions: **1a** (1 mmol), catalyst (10 mg, the ratio in parenthesis is the molar ratio of Ti to Mo), solvent (1 mL), air, irradiation under a 14 W CFL at room temperature for 4 h.

<sup>[b]</sup> Isolated yields.

<sup>[c]</sup> Reaction without catalyst.

<sup>[d]</sup> Reaction in the dark.

<sup>[e]</sup> 5 mg catalyst was used.

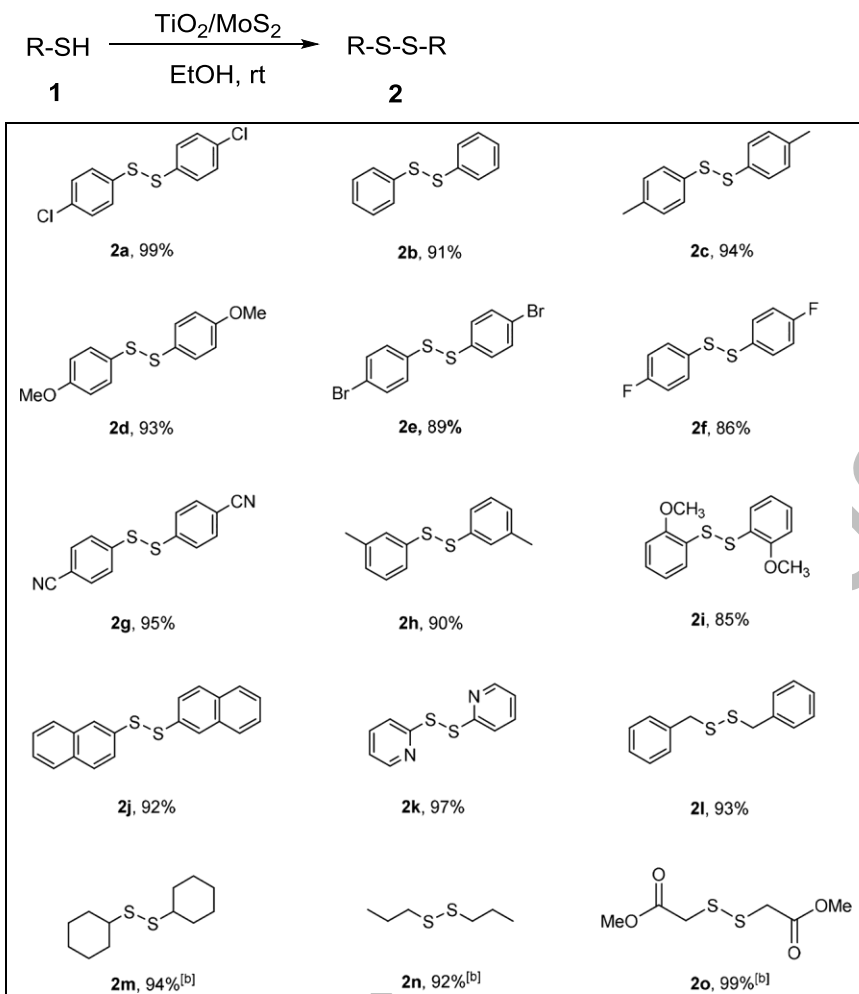
<sup>[f]</sup> 20 mg catalyst was used.

<sup>[g]</sup> N<sub>2</sub> atmosphere.

<sup>[h]</sup> O<sub>2</sub> atmosphere.

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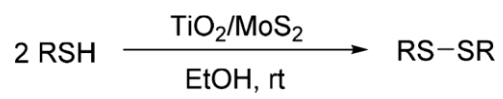
Table 2 Photocatalytic oxidation of various thiols



<sup>[a]</sup> Reaction conditions: **1** (1 mmol), TiO<sub>2</sub>/MoS<sub>2</sub> (10: 1 molar ratio) (10 mg), EtOH (1 mL), air, irradiation under a 14 W CFL at room temperature, isolated yields.

<sup>[b]</sup> Reaction time: 8 h.

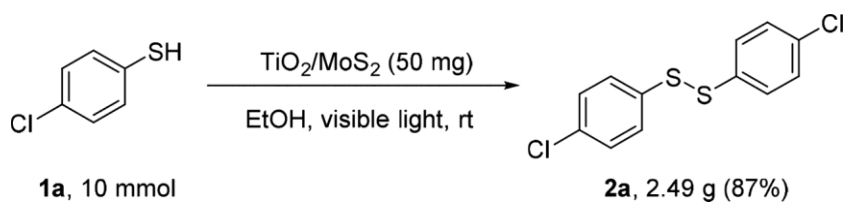
Scheme 1. Oxidative coupling of thiols in the presence of TiO<sub>2</sub>/MoS<sub>2</sub>



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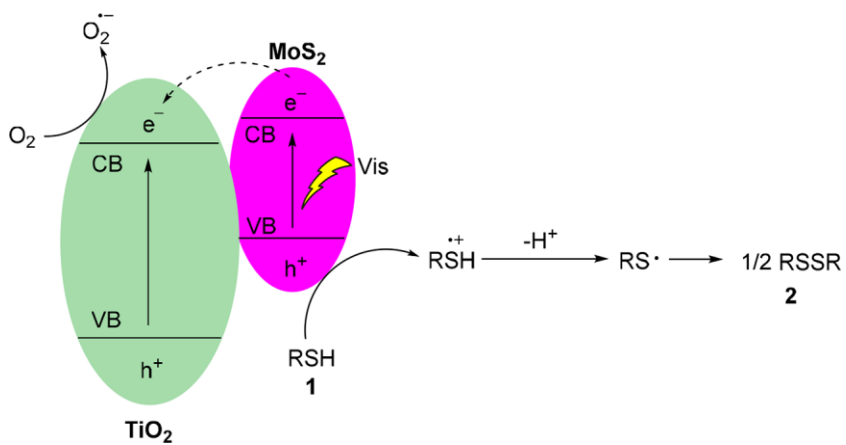


Scheme 2. Gram-scale synthesis of disulfide **2a**



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Scheme 3. Proposed mechanism



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