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Indium Oxide-Catalyzed Synthesis of Diaryl Disulfides from Aryl Halides

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Abstract

An efficient and general method for the synthesis of Aryldisulfides using indium (III) oxide as a catalyst is reported. Reaction of various organyl halides afforded the desired disulfide in good yields.

1. Introduction

Disulfide bonds are ubiquitous in many naturally occurring substances. For example, diallyl disulfide, ajoene, S-allylmercaptocysteine, and allicin are found in garlic.[1–4] These compounds have shown promising anti-infective properties.[5] Disulfides are also used in the synthesis of various organosulfur compounds.[6] Industrially, disulfides are employed as vulcanizing agents for rubbers and elastomers to increase their tensile strength.[7] Due to their importance, various strategies have been reported in the literature for the synthesis of disulfides. Among them, the oxidation of thiols to disulfides using various reagents and catalysts under controlled conditions is the most common.[8] Other methods include the conversion of alkyl halides to disulfides using Na_2S/S and the reductive coupling of sulfonyl chlorides.[9–10] However, these methods have several disadvantages. They often produce the desired disulfides along with solid waste by-products. Other drawbacks include the use of toxic reagents and metal oxidants, low yields, long reaction times, and high reaction temperatures.[11]

Thus, there exists a need for an efficient and simple method for the synthesis of disulfides without the formation of by-products. In this view, we have employed indium(III) oxide as a catalyst for the conversion of aryl halides into their corresponding disulfides. The method

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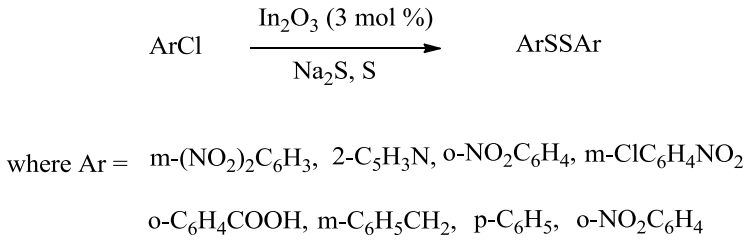
affords disulfides in good yields. The reaction is straightforward and involves simple work-up steps (Scheme 1).

Indium(III) oxide has been chosen as a catalyst for the following reasons:
i. It is an easily recyclable and reproducible catalyst.[12]
ii. It is active, stable, and non-toxic.[13]
iii. Indium(III) compounds are mild and water-tolerant.[14]
iv. Moreover, their application in organic transformations is still limited.[15]



Scheme 1. Synthesis of symmetrical disulfides.

2. Results and Discussions

In a general procedure, chlorobenzene (in ethanol) was refluxed with a solution of sodium disulfide (in ethanol) in the presence of varying amounts of catalyst. The effect of catalyst loading on the reaction system was examined. It was observed that when 3 mol% of the catalyst was used for the conversion of chlorobenzene to diphenyl disulfide, the yield of the desired product was high (78%). The results are summarized in Table 1.

Table 1: Effect of amounts of Indium (III) oxide on the synthesis of dipenyl disulfide

Entry	Substrate	Disulfide	Catalyst	Amount (mol %)	Yield[a] (%)
1	8a	8a	In_2O_3	1.0	25
2	8a	8a	In_2O_3	2.5	64
3	8a	8a	In_2O_3	3.0	78
4	8a	8a	In_2O_3	5.0	70
8	8a	8a	No catalyst	-	35

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Reaction conditions: A mixture of sulfur powder (0.16 g, 5 mmol), sodium sulfide (0.39 g, 5 mmol) and ethanol (10 ml) was stirred at room temperature for 15 min. The mixture was added to a solution containing substrate (6 mmol) and ethanol (10 ml) and 3 mol % of indium (III) oxide. The resulting mixture was refluxed for 48 min.

[a] Isolated yields. The potential of various solvents were also examined in the synthesis of diphenyl disulfide. Ethanol was found to be effective for the reaction system (Table 2).

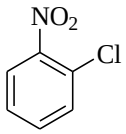
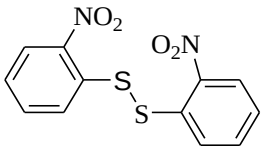
Table 2. Effect of various solvents on the synthesis of diphenyl disulfide

Entry	Substrate	Disulfide	Solvent	Yield[a] (%)
1	8a	8a	DMF	50
2	8a	8a	C_6H_6	39
3	8a	8a	CH_2Cl_2	55
4	8a	8a	CH_3Cl	60
5	8a	8a	C_2H_5OH	78

[a]Isolated yield

The protocol was extended for the conversion of several aromatic halides to their corresponding disulfides (Table 3). All were converted into corresponding disulfides giving good yields of the disulfides. Disulfides are the only products in the reaction condition.

Table 3. Synthesis of disulfides using In_2O_3 as catalyst

Entry	Substrate (**1**)	Product (**2**)	Reaction Time (min)	Melting Point (^{0}C)	Yield[a] (%)
1			30	193	85

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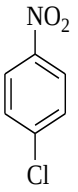
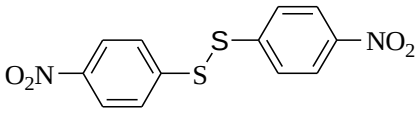
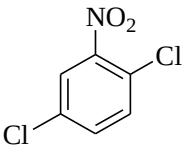
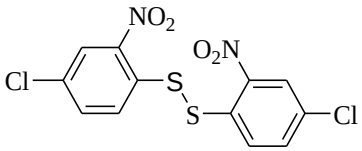
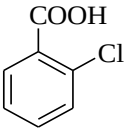
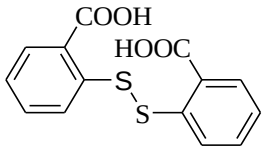
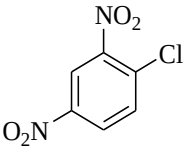
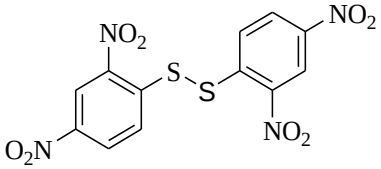
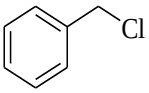
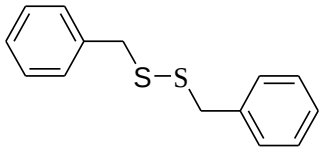
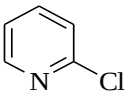
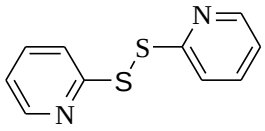
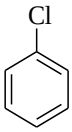
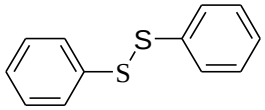
2			40	176	89
3			45	203	70
4			45	288	83
5			10	233	90
6			47	68	70
7			60	57	60
8			48	59	78

Reaction conditions: A mixture of sulfur powder (0.16 g, 5 mmol), sodium sulfide (0.39 g, 5 mmol) and ethanol (10 ml) was stirred at room temperature for 15 min. The mixture was added to a solution containing substrate (6 mmol) and ethanol (10 ml) and 3 mol % of indium (III) oxide. The resulting mixture was refluxed.

[a] Isolated yield.

Factors such as the presence of substituents in aryl chlorides influence the course of the reaction. For example, aryl chlorides containing nitro groups react rapidly to form the desired

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disulfides (entries 1, 2, and 5), while the presence of a chloro group in aryl chlorides decreases their reactivity toward disulfide formation (entry 3). On the other hand, aryl chlorides without substituents react more slowly (entries 6, 7, and 8).

It was also observed that the catalyst could be reused up to three times after washing with ethyl acetate or water, followed by drying under vacuum.

3. Conclusions

In conclusion, we have developed a new and efficient method for the synthesis of disulfides using indium(III) oxide as a catalyst. By applying this methodology, a variety of disulfides were synthesized in good yields.

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