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# A novel dual-nano assisted synthesis of symmetrical disulfides from aryl/alkyl halides

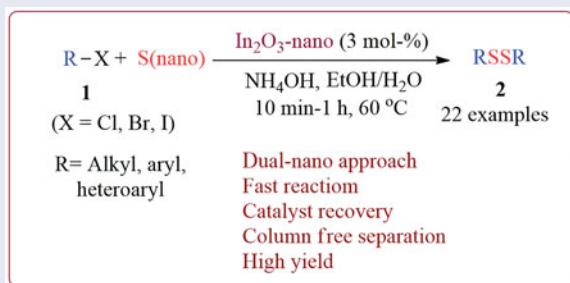
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## ABSTRACT

Here, we have reported a novel approach towards dual-nano assisted synthesis of disulfides from coupling of alkyl/aryl halides and sulfur nanoparticles. The indium oxide nanoparticles as catalyst expedite the conversion and sulfur nanoparticle notably enhances the miscibility, providing a faster, high yielding and cost-effective process in ethanol-water system. The method has synthetic advantages in terms of mild reaction framework, catalyst regeneration, and absence of any sulfide or polysulfide linkage as by-product leading to a column free synthesis. A variety of alkyl, aryl and heteroaryl symmetrical disulfides are obtained in good to excellent yields up to exceeding 98%.

## GRAPHICAL ABSTRACT



## ARTICLE HISTORY

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## KEYWORDS


Column-free separation; disulfide; dual-nano; green synthesis; recycle

## Introduction

The organic disulfides play a significant role in biological, chemical and industrial applications.<sup>[1]</sup> They are building blocks of organosulfur compounds,<sup>[1a,d,2]</sup> acceptable precursors for preparation of self-assembled monolayers and monolayer-protected clusters,<sup>[3]</sup> also partake in chemical substitution or addition reactions.<sup>[1b-d,2b,4]</sup> The S–S bond enclosed compounds act as important auxiliary functions in the synthesis of organic moieties such as  $\beta$ -hydroxythioethers via ring opening of epoxides,<sup>[5]</sup> 3-(arythio)indoles,<sup>[6]</sup> thia-Michael adducts<sup>[7]</sup> etc. Moreover, alkenes, alkynes, allenes,<sup>[4c]</sup>

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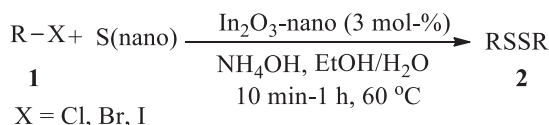
carbon monoxide, and thiocyanides can be inserted into sulfur–sulfur bonds to access a promisable method for the preparation of organosulfur compounds.<sup>[1c,8]</sup>

Oxidation of thiol is the primal method for synthesis of diorganoyl disulfides<sup>[9]</sup> although it accompany challenges of toxicity and pungent smell, excessive in aliphatic and heteroaryl thiols.<sup>[10]</sup> Compared to thiol, alkyl/aryl halides are easily available, odourless, cost effective and handling is much easier. Also, thiols are prepared from corresponding halides; hence, one-pot preparation of disulfides from halides can save both time and cost. Thus, attention has been drawn to utilize halides with sulfur sources such as alkali metal disulfides,<sup>[11]</sup> thiourea<sup>[12]</sup> and thiuronium salts,<sup>[13]</sup> thiocarboamide,<sup>[14]</sup> elemental sulfur,<sup>[15]</sup> and others.<sup>[16]</sup> But, the reactions mentioned with halides are often slower and moderate yielding due to many steps involved and usually affected at high temperature.<sup>[12c,17]</sup> Apart from it, nucleophilic sulfur sources with halides provide mixtures of substitution and fragmentation products making these reactions of scant synthetic value.<sup>[18]</sup>

Metal-nanoparticle can be an efficient catalyst in enhancing reactivity of these halide transformed reactions. Although green methodologies are overriding, metal catalysts gain excellent catalytic importance and many industrial processes are mainly metal assisted. Currently, nanostructured catalysts are used in organic reactions especially in coupling reactions, considering unidirectional or by-product bound synthesis. They furnish higher surface area and lower coordination sites responsible for its higher catalytic activity.<sup>[19]</sup> In addition, straightforward recovery and reuse of catalyst from the reaction mixture by simple filtration or centrifugation are considerable advantages.

Limited reports are known where sulfur and alkyl/aryl halides are directly used in disulfide preparation. Zhou *et al.* reported a Cu-phenanthroline catalysed method for synthesis of disulfide using phase transfer catalyst as additive under basic condition.<sup>[15b]</sup> Taniguchi reported a CuI-bpy catalyzed method for mono- and dichalcogenation of aryl halides.<sup>[15f]</sup> The method, although advantageous, required Al and MgCl<sub>2</sub> as additives and took sufficiently longer time for completion of the reaction at a high heat condition. Another report by Beigi and group described a MOF-199 catalysed transformation of aryl halides to disulfides in a strong basic condition at 130 °C.<sup>[15h]</sup> Thus, to get a mild reaction framework, we depicted a novel route over these extant halide transformed reactions. An InO-NP catalysed synthesis of disulfide from aryl/alkyl halides in ethanol-water system is reported here (Scheme 1).

The InO-NPs are stable enough, inexpensive and nontoxic heterogeneous catalysts with excellent reactivity. The nano-sized sulfur when compared to elemental sulfur shows yield intensification due to high miscibility<sup>[20]</sup> in ethanol-water system. Compared to reported methods of using aryl halides and sulfur, our synthetic route has notable advantages in terms of solvent selection, low catalyst load, high yield, faster reaction and recovery and reuse of the catalyst. Apart from it, nano-sulfur in disulfide synthesis is still unheard-of. This dual nano assisted method is a novel route to provide a by-product free transformation (absence of diaryl sulfide and diaryl polysulfides).



**Scheme 1.** General scheme for nano-catalyzed synthesis of disulfides.

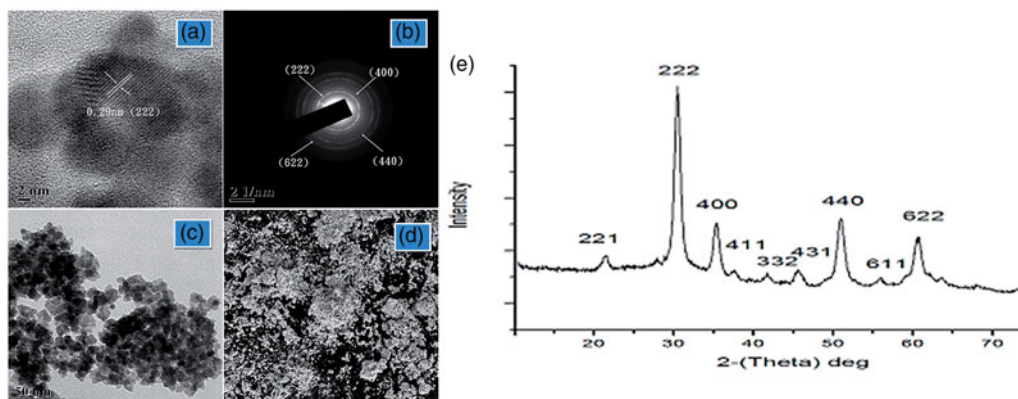
Various halides (R-X, X = Cl, Br, I) and its substituents provided excellent yields irrespective of its alkyl, aryl or heteroaryl nature. The heterogeneous nano catalysis and development of aqueous phase alcohol reactions also provide a green perspective.<sup>[21]</sup>

## Result and discussion

The In<sub>2</sub>O<sub>3</sub> nano-catalysts (particle size: 10–20 nm), were prepared from a synthetic hydrothermal method; the metal source was indium nitrate hydrate, dissolved in a tea extract of double-distilled water. The bio-extract in an ammonical solution expected to provide enough capping agent for stabilization of the synthesized nanoparticles through steric hindrance, preventing their aggregation.<sup>[22]</sup> The after dried pale-white precipitate over calcination (400 °C) turned pale yellow and used for spectral analyses. The native InO-NPs were analysed through powder XRD (X-ray diffraction), SEM (scanning electron microscope) and TEM (transmission electron microscopy) study (Figure 1). The synthesized InO-NPs were further used as catalyst in disulfide preparation.

For optimization, bromobenzene and sulfur powder were selected as model substrates and various parameters were optimized to develop its scope. Primarily, the reaction was performed using a stoichiometric ratio of bromobenzene (1 mmol) and sulfur powder (2 mmol) in ammonical acetonitrile medium (5–10 ml) in presence of nano indium oxide (2 mol-%). The sulfur powder had low miscibility in this reaction and even after continuous stirring for 5–6 h, only a faint spot on TLC could be observed (Table 1, entry 1). The increase in temperature up to 60 °C for about 12 h could not significantly enhance the productivity (Table 1, entry 2). Hence, we synthesized S-NPs using a reported method<sup>[23]</sup> among available literatures<sup>[24]</sup> and carried out further reactions. The S-NPs are easily synthesized, exhibit low chemical reactivity towards organic compound and a wide range of reactive functionalities remain intact in the presence of sulfur. In addition, water soluble property of nano-sulfur is a notable advantage over ordinary sulfur,<sup>[20]</sup> to avoid organic solvents.

A list of trials was performed under different concentrations, bases and different solvents to get optimized reaction condition (summarized in Table 1). The nano-sulfur (2 mmol) with bromobenzene (1 mmol) and nano indium oxide (2 mol-%) in ammonical

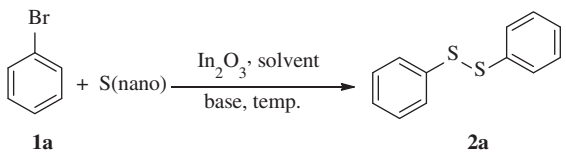


**Figure 1.** (a) HR TEM image showing the lattice fringes; (b) SAED pattern; (c) TEM image of aggregated; (d) FE SEM image; (e) Powder XRD.

acetonitrile (5–10 ml) enhances the productivity (50%) proving its effectiveness (Table 1, entry 3). However, the yield was not as good as expected. Changing the solvent system to ethanol and maintaining substrate ratio of bromobenzene: sulfur = 1.0:3.0, the reaction intensifies the yield up to ~64% (entry 4). A 2:1 solution of ethanol: water further enhances the yield up to 72%, (entry 5) whereas 1:1 ratio diminishes. The maximum yield was obtained when bromobenzene (1.2 mmol) was treated to S-NPs (3 mmol) with an increased catalyst load of (3 mol-%) in a 2:1 ratio of EtOH:H<sub>2</sub>O at 60 °C (entry 6). Further increase in catalyst load (5 and 8 mol-%) merely have any impact on the reaction (entry 7) proving 3 mol-% as sufficient catalyst load. The influence of catalyst load and its impact on the yield is shown in Table 2.

We also examined effect of various metal catalysts on the S–S bond formation (Table 3). It was found that nanoparticles were quite more effective compared to the

**Table 1.** Optimization of reaction conditions.



Reaction scheme: **1a** (bromobenzene) + S(nano)  $\xrightarrow[\text{base, temp.}]{\text{In}_2\text{O}_3, \text{ solvent}}$  **2a** (disulfide)

Entry	1a:Sulfur (mmol)	Solvent	Base	Temp (°C)	Time (h)	Yield (%) <sup>[b]</sup>
1 <sup>[c,d]</sup>	1.0:2.0	CH <sub>3</sub> CN	NH <sub>4</sub> OH	RT	6	Trace
2 <sup>[c,d]</sup>	1.0:2.0	CH <sub>3</sub> CN	NH <sub>4</sub> OH	60	12	35
3	1.0:2.0	CH <sub>3</sub> CN	NH <sub>4</sub> OH	60	6	50
4 <sup>[d]</sup>	1.0:3.0	EtOH	NH <sub>4</sub> OH	60	2	64
5 <sup>[d]</sup>	1.0:3.0	EtOH/H <sub>2</sub> O (2:1)	NH <sub>4</sub> OH	60	2	72
6 <sup>[a]</sup>	<b>1.2:3.0</b>	<b>EtOH/H<sub>2</sub>O (2:1)</b>	<b>NH<sub>4</sub>OH</b>	<b>60</b>	<b>0.5</b>	<b>92</b>
7 <sup>[e]</sup>	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	NH <sub>4</sub> OH	60	0.5	93
8 <sup>[d]</sup>	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	NH <sub>4</sub> OH	RT	24	38
9	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	NH <sub>4</sub> OH	80	0.5	93
10	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	NH <sub>4</sub> OH	110	0.5	88
11	1.2:3.0	H <sub>2</sub> O	NH <sub>4</sub> OH	80	24	–
12	1.2:3.0	DMF	NH <sub>4</sub> OH	60	3	49
13	1.2:3.0	Dioxane	NH <sub>4</sub> OH	60	24	–
14	1.2:3.0	Toluene	NH <sub>4</sub> OH	60	3	38
15	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	K <sub>2</sub> CO <sub>3</sub>	60	3	42
16	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	<i>t</i> -BuOK	60	3	34
17	1.2:3.0	EtOH/H <sub>2</sub> O (2:1)	KOH	60	3	32

Note. The bold values represents optimized condition for disulfide synthesis.

<sup>[a]</sup>Optimized reaction condition: bromobenzene (1.2 mmol), nano-sulfur powder (3.0 mmol), indium source (3 mol-%), NH<sub>4</sub>OH (1.0 mmol), ethanol-water (2:1, 2–5 mL), stirred for 0.5 h, 60 °C.

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

<sup>[c]</sup>Elemental sulfur (3 mmol).

<sup>[d]</sup>Indium source (2 mol-%).

<sup>[e]</sup>InO-NP (8 mol-%).

**Table 2.** Catalyst load (indium (oxide, In<sub>2</sub>O<sub>3</sub>) screening for S–S coupling<sup>[a]</sup>.

Entry	In <sub>2</sub> O <sub>3</sub> (mol-%)	Yield <sup>[b]</sup> (%) <sup>[b]</sup>
1	1	64
2	2.0	78
3	<b>3.0</b>	<b>92</b>
4	5.0	92
5	8.0	93

Note. The bold values represents optimized condition for catalyst load in disulfide synthesis.

<sup>[a]</sup>Bromobenzene (1.2 mmol), S-NP (3.0 mmol), NH<sub>4</sub>OH (1.0 mmol), solvent (2–5 mL), 60 °C.

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

**Table 3.** Evaluation of different metal catalysts for the formation of diphenyl disulfide<sup>[a]</sup>.

Entry	Halide	Product	Metal nano catalyst	Yield (%) <sup>[b]</sup>
1	Ph-Br	Ph <sub>2</sub> S <sub>2</sub>	ZnO	54
2	Ph-Br	Ph <sub>2</sub> S <sub>2</sub>	NiO	66
3	Ph-Br	Ph <sub>2</sub> S <sub>2</sub>	In <sub>2</sub> O <sub>3</sub>	92
4 <sup>[c]</sup>	Ph-Br	Ph <sub>2</sub> S <sub>2</sub>	In <sub>2</sub> O <sub>3</sub>	64
5 <sup>[d]</sup>	Ph-Br	Ph <sub>2</sub> S <sub>2</sub>	NiL <sub>2</sub>	73
6 <sup>[d]</sup>	Ph-Br	Ph <sub>2</sub> S <sub>2</sub>	PdL <sub>2</sub>	60
7			–	0
8	4-MePhBr	(4-MePh) <sub>2</sub> S <sub>2</sub>	ZnO	60
9	4-MePhBr	(4-MePh) <sub>2</sub> S <sub>2</sub>	NiO	71
10	4-MePhBr	(4-MePh) <sub>2</sub> S <sub>2</sub>	In <sub>2</sub> O <sub>3</sub>	96
11 <sup>[c]</sup>	4-MePhBr	(4-MePh) <sub>2</sub> S <sub>2</sub>	In <sub>2</sub> O <sub>3</sub>	68
12 <sup>[d]</sup>	4-MePhBr	(4-MePh) <sub>2</sub> S <sub>2</sub>	NiL <sub>2</sub>	78
13 <sup>[d]</sup>	4-MePhBr	(4-MePh) <sub>2</sub> S <sub>2</sub>	PdL <sub>2</sub>	66

<sup>[a]</sup>Aryl halide (1.2 mmol), S-NP (3.0 mmol), metal source (3 mol-%), NH<sub>4</sub>OH (1.0 mmol), solvent (2–5 mL), 60 °C.

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

<sup>[c]</sup>Indium metal oxide.

<sup>[d]</sup>Metal complex.

metal salts. However, among various metal nano particles, In<sub>2</sub>O<sub>3</sub> found to be the most effective catalyst in disulfide synthesis. Some of our synthesized and reported metal complexes of Ni and Pd were also tried;<sup>[25]</sup> we noticed its high catalytic reactivity, but lower than InO-NPs. The reaction stopped in the absence of metal catalyst (Table 3, entry 7), indicating high importance of the metal center.

From the monitoring of solvent, base and catalyst we considered entry 6, Table 1 as the optimum reaction condition. The TLC monitoring showed full conversion of aryl halide to disulfide unlike earlier methods which often suffered from by-products of sulfides or polysulfides. Polysulfide is usually avoided by employing a co-catalyst.<sup>[19]</sup> However, in this report use of nano-sized sulfur or dual-nano possibly effect the reaction condition to give disulfide as the single major product. The synthesis of **2a** took almost 0.5 h for completion and structurally confirmed by both <sup>1</sup>H and <sup>13</sup>C NMR as well as HRMS analysis (Supporting information).

The substrate scope analysis under optimized reaction condition showed that, the method is tolerant to various aryl halides i.e. chloride, bromide or iodide. The aryl bromides and iodides having both electron releasing and electron withdrawing substituent in the ring gave slightly better yield of disulfides compared to their chloro analogues (Table 4, entries 1–3, 20). A variety of substituted and unsubstituted aryl (Table 4, entries 1–17), heteroaryl, (Table 4, entries 18–20), and alkyl iodide (Table 4, entry 21–22) were successfully converted to corresponding disulfides with excellent yields. Introducing the methyl, methoxy, nitro, amino, acetyl and halo group to the aryl halide afforded good yield of product. The donating groups on aryl halides exhibit slightly better reactivity compared to unsubstituted or electron withdrawing groups in it. The reaction rates of the alkyl iodide and heteroaryl iodide are much lower than those of other aryl iodides. The maximum yield (>98%) could be obtained in case of 4-methyl substituted aryl iodide (Table 4, entry 5). The reactions described above are clean, safe and high yielding. Depending on substituents, it took almost 10 min–1 h for completion. Electron donating substituents on the aryl halides exhibit comparatively faster reactions.

**Table 4.** Synthesis of disulfides<sup>[a]</sup>.

Entry	RX (1)	RSSR (2)	Yield (%) <sup>[b]</sup>
1	Ph-	2a	94 (X = I) 92 (X = Br) 89 (X = Cl)
2	PhCH <sub>2</sub> -	2b	92 (X = Br) 88 (X = Cl)
3	2-NH <sub>2</sub> Ph-	2c	91 (X = I) 89 (X = Br) 85 (X = Cl)
4	2-MePh-	2d	95 (X = I) 94 (X = Br)
5	4-MePh-	2e	>98 (X = I) 96 (X = Br)
6	4- <sup>t</sup> BuPh	2f	90 (X = I)
7	3-MeOPh-	2g	90 (X = I)
8	4-MeOPh-	2h	95 (X = I)
9	4-Acetyl Ph-	2i	88 (X = I)
10	3-Cl Ph-	2j	91 (X = I)
11	4-Cl Ph-	2k	89 (X = I) 89 (X = Br)
12	4-FluoroPh-	2l	80 (X = I)
13	2-NO <sub>2</sub> Ph-	2m	84 (X = I)
14	4-NO <sub>2</sub> Ph-	2n	86 (X = I) 84 (X = Br)
15	2,4-dinitrophenyl	2o	76 (X = I)
16	2-Naphthyl-	2p	88 (X = I)
17	2-carboxyphenyl	2q	82 (X = I)
18	2-Pyridyl-	2r	82 (X = I)
19	3-Pyridyl-	2s	86 (X = I) 84 (X = Br)
20	5-Br-2-pyridyl-	2t	82 (X = I) 81 (X = Br) 76 (X = Cl)
21	Cyclohexyl	2u	89 (X = I) 87 (X = Br)
22	n-Butyl-	2v	80

<sup>[a]</sup>Aryl/alkyl halide (1.2 mmol), S-NP (3.0 mmol), InO-NP (3 mol-%), NH<sub>4</sub>OH (1.0 mmol), solvent (2–5 mL), 60 °C.

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

To check recyclability of the catalyst, InO-NPs were separated from reaction mixture by careful ultracentrifugation, washed several times with water, dried under vacuum and reused for further catalytic reactions. The recovered catalyst was reused under similar conditions for subsequent run and the catalytic behaviour of InO-NPs were found to be unaltered up to minimum five consecutive cycles (Table 5).

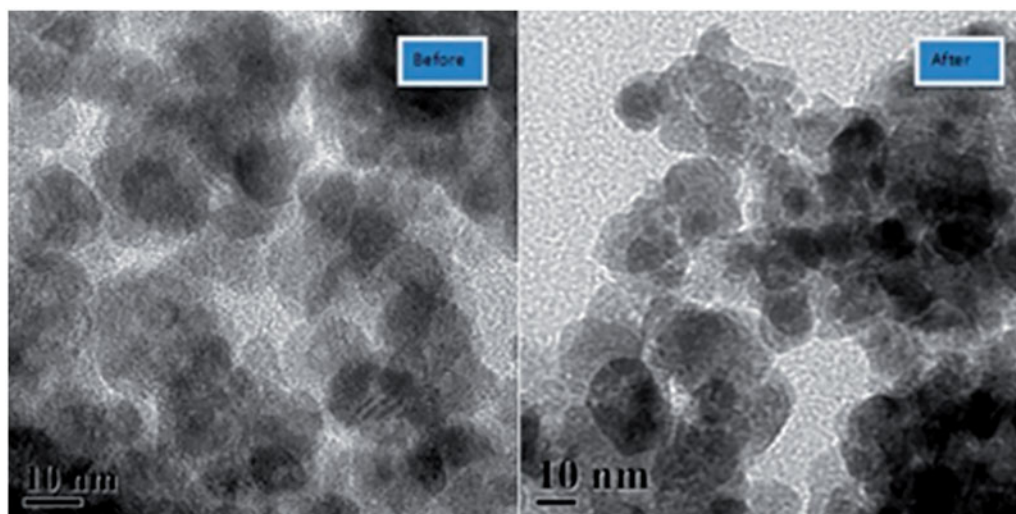
The TEM (Figure 2) images of the fresh and recovered catalyst after the 5th cycle showed that the morphology of the catalyst remained unaltered. The catalytic action however after fifth cycle showed gradually diminished activity and maximum 68% of disulfide could be generated after 8th catalytic run. The diminished reactivity can be explained in terms of possible metal leaching from the released acid (Scheme 2) upon repeated use of metal nanoparticles, which is normally prevented by neutralizing the acid with an ammonical solution. The involvement of the substrates and the catalyst in

**Table 5.** Recyclability of nano  $\text{In}_2\text{O}_3$ <sup>[a]</sup>.

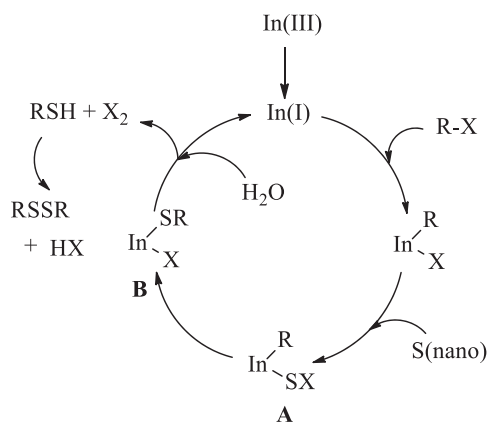
No. of cycle	Catalyst recovery (%)	Yield(%) <sup>[b]</sup>
1	96	94
2	93	92
3	90	91
4	90	91
5	86	90

<sup>[a]</sup>Bromobenzene (1.2 mmol), S-NP (3.0 mmol),  $\text{InO-NP}$  (3 mol-%),  $\text{NH}_4\text{OH}$  (1.0 mmol), solvent (2–5 mL), 60 °C.

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



**Figure 2.** TEM images of the fresh catalyst (left) and the catalyst after 5th cycle (right).



**Scheme 2.** Plausible mechanism.

the performance of disulfide synthesis is explained by the plausible mechanism shown in [Scheme 2](#).

The nano indium oxide advances binding of aryl halide on its surface<sup>[26]</sup> and S(nano) is incorporated in an intermediary step forming **A**. The intermediate **A**



**Table 6.** Control experiment for mechanism investigation<sup>[a]</sup>.

Sl no	Substrates (R = Ph, R' = 4-ClPh)	Metal nano	Oxidant	Product	Yield (%) <sup>[b]</sup>
1	RSH	In <sub>2</sub> O <sub>3</sub>	–	–	–
2	RSH	In <sub>2</sub> O <sub>3</sub>	X <sub>2</sub> (X = I or Br)	RSSR	76
3	R-X + S	–	X <sub>2</sub>	–	–
4	R-X + S	In <sub>2</sub> O <sub>3</sub>	–	RSSR	92
5	R-X + S + R'SH	In <sub>2</sub> O <sub>3</sub>	–	RSSR + R'SSR'	Mixture of disulfides

<sup>[a]</sup>Aryl halide (1.2 mmol), S-NP (3.0 mmol), InO-NP (3 mol-%), NH<sub>4</sub>OH (1.0 mmol), solvent (2–5 mL), 60 °C.

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

possibly undergoes transformation to form **B** in a subsequent step. In presence of ethanol-water, the reaction generates thiol. The molecular halogen released from aryl/alkyl halide, oxidizes thiol to the corresponding disulfide. Respective thiol must be generated in the intermediate step, as absence of protic solvent especially water in the solvent system reduces the reaction rate and productivity. In presence of water, indium is reduced to complete the catalytic cycle. The release of HX and simultaneous formation of disulfide can be possible if only thiol formed as intermediate. If the reaction directly produce sulfenyl halide (RSX) as an intermediate from **A**, the reaction should liberate molecular halogen as a recoverable by-product, which is not the case. Thus, the reaction possibly follows [Scheme 2](#).



A series of reactions were tested to prove the mechanism ([Table 6](#)); Addition of 4-chlorothiophenol from outside could generate bis-(4-chlorophenyl) disulfide along with diphenyl disulfide which proves the release of halogen inside.

Experiments between aryl iodide and sulfur in presence of catalyst and a radical scavenger [2,2,6,6]-tetramethylpiperidine-N-oxyl (TEMPO) or hydroquinone under standard optimized condition, showed that the reactions were not affected in terms of yield. It clearly indicates the unlikely nature of the reaction to proceed through radical formation.

## Experimental section

### Materials and methods

All solvents and chemicals were purchased commercially and used without further purification. Melting points were recorded on an electro thermal digital melting point apparatus and were uncorrected. <sup>1</sup>H and <sup>13</sup>C Nuclear Magnetic Resonance spectra of pure compounds were acquired at 400 and 100 MHz, respectively. The NMR samples were recorded in deuterated chloroform. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Elemental analyses were performed on a Flash 2000 Thermo Scientific instrument. The TEM and SEM characterization were carried out at model no. CM-12 Philips TEM (IIT Kharagpur) and FEI Nova nano SEM-450 (NIT Rourkela), respectively.

## Procedures

### *Synthesis of sulfur nanoparticles, S-NPs; general procedure<sup>23</sup>*

Elemental sulfur powder (1 g) was taken in a silica crucible and heated in an oven preset at 120 °C for 25 min. The melted substance was brought down to room temperature and then placed over an ice bath. Finally, it was grinded with mortar and pestle. This process was repeated thrice. After that, it was washed with double distilled water (3 × 15 mL) and dried in oven at 100 °C.

### *Synthesis of indium oxide nanoparticles; general procedure*

In a typical procedure, 0.01 mole indium nitrate hydrate was dissolved in a tea extract solution, (10g of Red Label tea in 100mL double-distilled water boiled at 80 °C for 10 min before decanting) was stirred for 30 minutes at the temperature 60 °C. After cooling to room temperature ammonia (25 wt-%) was added drop by drop to the solution to achieve a final pH 10. The resulting solution was dried at 50 °C overnight to get pale-white precipitate, which was centrifuged; filtered and finally calcined at 400 °C for one hour.

### *Synthesis of disulfide, 2a–2v; general procedure*

A mixture of alkyl/aryl halide, **1** (1.2 mmol), ammonium hydroxide (1 mmol) and nano-sulfur powder (3 mmol, 96 mg) was stirred in 5 mL of solvent (ethanol/water (2:1)) at 60 °C. Under this stirring condition indium oxide nanoparticles (3 mol-%) were added to it and the reaction was stirred for a period of 10min to 1 h at 60 °C. After completion of the reaction as indicated by thin layer chromatography (TLC), the reaction mixture was cooled to room temperature and a 2:1 mixture of ethyl acetate/water (15 mL) was added and indium oxide was removed by centrifuge. The combined organic extracts were dried with anhydrous sodium sulfate and concentrated to give desired product in high purity.

## Conclusions

In summary, a dual nano-effect has been focused in this manuscript and successfully applied in the synthesis of symmetrical disulfides. Various conditions were optimized and outcomes are fully explained here. An attempt of green approach is justified by performing the reaction in a benign solvent mixture of ethanol-water and in terms of enhanced reactivity by the use of both nano indium oxide and nano-sulfur reagent. Nano indium oxide has an excellent catalytic behaviour in terms of reactivity, reducing reaction time, and increasing productivity. The novelty of this reaction lies in the complete conversion of halides to disulfides (yield exceeding 98%) without forming any side product, e.g. aryl sulfide or polysulfide linkages. Again, easy recovery and reusability of this catalyst without loss in activity makes this method a practically applicable one.

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## Declaration of interest

No potential conflict of interest was reported by the authors.

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