

Ni-nanoparticles: An efficient green catalyst for chemo-selective oxidative coupling of thiols

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Abstract

Use of highly monodispersed, easily recyclable and cheap nickel nanoparticles for oxidative coupling of aliphatic, aromatic, cyclic and heteroaromatic thiols to their corresponding disulfides has been reported. Ni-nanoparticles act as a green catalyst that can selectively catalyse oxidative coupling of thiols to disulfides without producing any over-oxidized products. The catalytic reaction occurred at room temperature with excellent yield under air atmosphere and high TON and TOF value could be achieved. Effect of solvent polarity and size distribution of the Ni-nanoparticles on the catalytic efficiency have been investigated. Nickel nanoparticles could be easily recovered by mild centrifugation.

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Keywords: Ni-nanoparticles; Green catalyst; Thiols; disulfides; Catalytic oxidation

1. Introduction

Oxidative coupling of thiols to disulfides is of interest from biological, synthetic and oil-sweetening point of view [1–6]. Since thiol can be over oxidized, extensive research has been carried out in recent years to control their oxidation [7–12]. Most of the existing methods involve the use of reagents such as molecular oxygen [13], metal ions [14], $\text{Bu}_3\text{SnOMe}/\text{FeCl}_3$ [15], nitric oxide [16], halogens [17–20], sodium perborate [21], borohydride exchange resin (BER)-transition metal salt system [22], a morpholine iodine complex [23], picolinium chlorochromate (PCC) [24], ammonium persulfate [25], $\text{KMnO}_4/\text{CuSO}_4$ [26], H_2O_2 [27], solvent free permanganate [28], $\text{PVP-N}_2\text{O}_4$ [29] and cesium fluoride–celite, $-\text{O}_2$ [30]. Some of these methods suffer from one or more of disadvantages such as long reaction times, difficult workup, lack of general applicability to thiol substrates bearing alkyl, aryl, cyclic and heteroaromatic moieties, formation of over-oxidation products leading to lower yields, use of stoichiometric excess amounts of the reagents for successful oxidation, requirements of strong oxidizing agents, strong acidic or basic media, and use of expensive

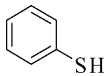
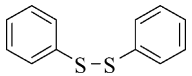
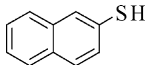
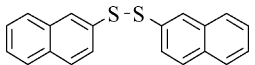
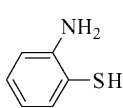
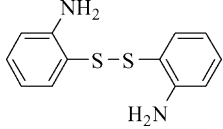
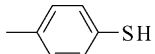
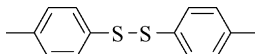
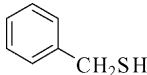
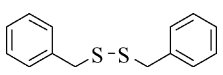
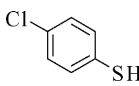
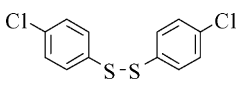
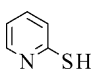
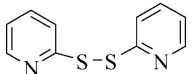
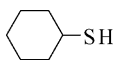
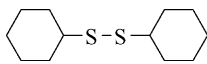
reagents. The oxidation of thiols to disulfides is a characteristic reaction [30–36] and further oxidation to disulfide S-oxides (thiosulfonates), 1,1-dioxides (thiosulfonates), and sulfonic acids are possible. Weak S–S bonds in these compounds impart high reactivity [37] and in natural products these moieties and related cyclic analogues are associated with interesting biological activities including DNA-cleaving properties [38,39]. In recent years, there has been growing interest in the catalytic properties of transition metal nanoparticles [40]. The high surface area-to-volume ratio of solid-supported metal nanoparticles [41] is mainly responsible for their catalytic properties and this can be exploited in many industrially important reactions [42]. Recent literature shows that nanoparticles have hardly been used as catalysts in organic synthesis. Ni-nanoparticles, in particular, being cheap, require only mild reaction conditions for high yields of products in short reaction times as compared to traditional catalysts.

Thus, there is still a need to develop a mild and efficient methodology of synthesizing aliphatic, aromatic, and heteroaromatic disulfides. In the continuation of our work on new applications of nanoparticles [43–45] in catalysis, we wish to further disclose an efficient and rapid protocol using monodispersed, cheap, easily recyclable Ni-nanoparticles as a chemo-selective catalyst for the oxidative coupling of various thiols to their corresponding disulfides under ambient conditions.

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Table 1
Oxidation of thiols to disulfides using 15 mol% nickel nanoparticles and acetonitrile as solvent at room temperature^{a,b}

Entry	Reactants	Product	Reaction time (min)	Yield	mp or bp (mmHg °C) (found)
a			6	98	57–60
b			8	93	141–143
c			11	94	75–76
d			9	98	46–47
e			4	96	69–70
f			12	85	72–73
g			8	91	127–129
h	CH ₃ (CH ₂) ₃ -SH	CH ₃ (CH ₂) ₃ -S-S-(CH ₂) ₃ CH ₃	9	90	94–96
i	CH ₃ (CH ₂) ₇ -SH	CH ₃ (CH ₂) ₇ -S-S-(CH ₂) ₇ CH ₃	15	95	201–203
j			10	92	123–126
k	SH-CH ₂ -CH ₂ -SH	-(S-CH ₂ -CH ₂ -Sn)-	35	91	–

^a Confirmed by comparison with authentic samples (FT-IR, H NMR, C NMR, mass-analysis, TLC, mp, bp).

^b Yield of isolated pure product after chromatography/distillation and recrystallization.

Catalysis through nanoparticles is a well-established process. The ability of the nanoparticles to catalyze the chemical reaction depends on many factors, such as—size, shape, electronic structure, surface area, etc. Our process is highly economic and eco-friendly as it requires neither elevated temperature, nor harsh acids or bases, produces high yield with excellent chemo-selectivity, reduces the reaction time and is applicable to variety of aliphatic, aromatic, cyclic and heterocyclic thiols substrates. Moreover, it is a one-pot synthesis that does not require inert atmosphere, has an easy work up and product isolation from the catalyst. In contrast, when Raney nickel or other complexes are used as catalysts an excessive amount of catalysts (usually in grams which may trigger toxicity) is typically found in the form of waste after the reaction [46–49]. This has been significantly reduced to microgram (less chances of exhibiting toxicity) using our methodology viz. using nickel nanoparticles. As far as toxicity of nickel nanoparticles are concerned there are many reports in which nickel nanoparticles have been used for various applications including *in vivo* and *in vitro* treatment of living cells/organisms and no evidence of toxicity has been reported at a low level of dosage [50,51]. Therefore, we claim that our method is much more ecofriendly and less toxic.

2. Results and discussion

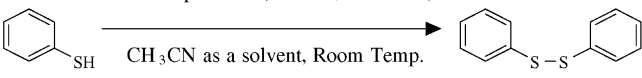
To understand the possible mechanism of the Ni-nanoparticles mediated oxidative coupling a control experiment was conducted in the absence of a catalyst and it was observed that no reaction occurred. However, the presence of Ni-nanoparticles is not only the limiting factor, but the presence of O₂ is also absolutely necessary for the oxidation of thiols as no reaction proceeded under N₂ atmosphere. As evident from the above-mentioned observation it can be proposed that Ni-nanoparticles are extremely active and provide enormous surface area that uses molecular oxygen as an oxidant for the oxidation of thiols. It is apparent from the data (Table 1) that all aliphatic, aromatic, cyclic and heteroaromatic thiols underwent the reaction smoothly. The presence of electron withdrawing/donating groups had negligible effect on the yield but had some influence on the rate of the reaction.

2.1. Catalyst concentration

The effect of catalyst (Ni-nanoparticles) concentrations on the reaction rate and yield of the product was also investigated (Table 2). It was found that the optimum reaction rate and yield

Table 2
Effect of catalyst concentration on yield of the product and reaction time

Ni-nanoparticles (x mol%, 15–18 nm)
CH₃CN as a solvent, Room Temp.



Entry	Catalysts (x, mol%)	Yield (%)	Reaction time (min)
1	2	18	17
2	5	50	15
3	8	65	13
4	10	84	10
5	15	94	6
6	18	94	6
7	20	93	6
8	25	94	6

could be achieved at the catalyst concentration of 15 mol% with the thiol concentration kept constant.

2.2. Effect of particles size on the catalytic efficiency

Ni-nanoparticles of sizes ranging from 10 nm to 85 nm in diameters were prepared in the aqueous cores of the reverse micellar droplets. The catalytic efficiency of the nanoparticles was found to be dependent on the size of the nanoparticles (Table 3). The maximum conversion was obtained for particles in average diameter of about 20 nm. Particles below this diameter exhibited a trend of decreasing reaction rate with the decrease in particle size, while those above this diameter showed a steady decline of reaction rate with increasing size. It has been postulated that in the case of particles smaller than 20 nm in average size, a downward shift of Fermi level with a consequent increase in band gap energy takes place. As a result, the particles require more energy to pump electrons to the adsorbed ions for the electron transfer reaction. This leads to a reduced reaction rate catalyzed by smaller particles. On the other hand, for nanoparticles larger than 20 nm in diameter, the change of Fermi level is not appreciable. However, these particles with larger size exhibit less surface area for adsorption. As a result, the catalytic efficiency of the particles is also decreased with increasing particle size.

2.3. Solvent effect

The oxidative coupling of thiols was also investigated in various solvents such as CH₃CN, CHCl₃, CH₂Cl₂, THF and

Table 3
Effect of size of the Ni-nanoparticles on catalytic oxidative coupling of Thiophenol and 2-aminothiophenol using 15 mol% Ni-nanoparticles at room temperature under air atmosphere^a

Particle size (±2 nm)	Thiophenol		2-Aminothiophenol	
	Yield (%)	Time (min)	Yield (%)	Time (min)
10	89	10	87	12
20	95	6	93	8
30	93	9	89	15
85	71	22	62	25

^a Acetonitrile was used as solvent in all the reactions.

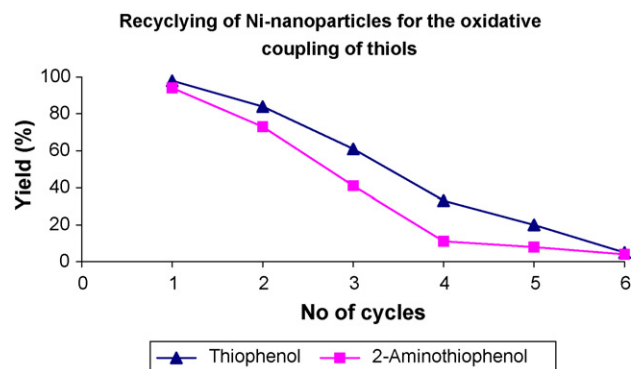


Fig. 1. Effect of recycling of Ni-nanoparticles on catalytic oxidative coupling of Thiophenol and 2-aminothiophenol using 15 mol% Ni-nanoparticles at room temperature stirred under air atmosphere. Acetonitrile was used as solvent.

n-hexane with all the other parameters kept constant and the progress of the reaction was checked through TLC. The yields were found to be 96, 75, 40, 32 and 8%, respectively. Hence, CH₃CN was used for all the reactions through the work. The nanoparticles thus prepared could be stored in absolute ethanol or as dry powder under N₂ atmosphere for a long period. The advantage of the nanoparticles is that unlike other catalyst, their use is not restricted by their solubility, as the nanoparticles can be dispersed in desired solvent by agitation or slight sonication.

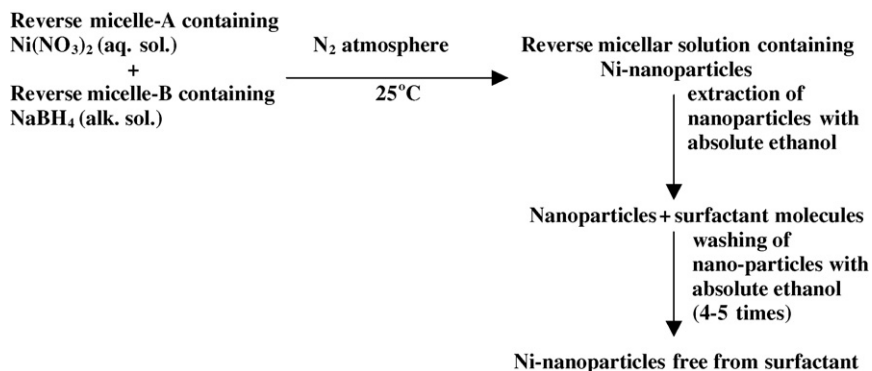
2.4. Recyclability

After the completion of the reaction the Ni-nanoparticles were recycled by separating them from the reaction mixture by mild centrifugation at 2000–3000 rpm and used as a catalyst for the same reaction again. It was observed that with increasing numbers of cycles the catalytic activity of the Ni-nanoparticles decreased and that it was nearly lost after six cycles, as shown in (Fig. 1). This may be explained on the basis of slow but continuous oxidation of nickel nanoparticles during the course of reaction.

3. Experimental

3.1. General information

The materials were purchased from Sigma–Aldrich and Merck and were used without any additional purification. All reactions were monitored by thin layer chromatography (TLC) on gel F254 plates. The silica gel (250–400 meshes) for column chromatography was purchased from Spectrochem Pvt. Ltd. India. ¹H NMR (300 MHz) and ¹³C NMR (300 MHz) spectra were recorded on a Bruker Spectrospin 300 MHz spectrometer in CDCl₃ (with TMS for ¹H and CDCl₃ for ¹³C NMR as internal references). MS were recorded on a TOF-Mass spectrometer Model No. KC455. Melting points were recorded on a Buchi melting point 540 instrument. The size and morphology of Ni-nanoparticles were characterized with the help of a transmission electron microscope (TEM, FEI Philips Morgagni 268Dmodel) Acc. voltage: 100 kV with magnification:



Scheme 1. Preparation of nickel nanoparticles.

up to 280,000) and a Quasi Elastic Light Scattering instrument (QELS, photacor-FC, model-1135 P) and the metallic nature of the particles was confirmed with a UV-spectrophotometer (Shimadzu).

3.2. Preparation of nanoparticles

A chemical method involving reduction of Ni^{2+} ions to $\text{Ni}(0)$ in a reverse micellar system was employed to prepare the nickel nanoparticle (Scheme 1). Poly (oxy ethylene)(tetra methyl butyl)-phenyl ether, commercially known as TritonX-100 (TX-100) was used as the surfactant, cyclohexane as the solvent (continuous phase), hexanol as co-surfactant and aqueous solution of salts as dispersed phase (water core in which particles formation occurs).

The reverse micelles were prepared by dissolving TX-100 in cyclohexane (usually 0.08–0.15 M of TX-100 solution). A typical preparative method is as follows:

To 100 ml of (0.1 M TX-100 solution in cyclohexane) 900 μl of $\text{Ni}(\text{NO}_3)_2$ aqueous solution (2%, w/v) and hexanol (q.s.) was added to afford an optically clear reverse micellar solution (RM-1). To another 100 ml of (0.1 M TX-100 solution in cyclohexane) NaBH_4 solution (5%, w/v in 2% NaOH (w/v) aqueous solution) and hexanol (q.s.) was added to afford RM-2.

To the prepared reverse micellar solution of $\text{Ni}(\text{NO}_3)_2$ aqueous solution (2%, w/v) (RM-1), another reverse micel-

lar NaBH_4 solution (5%, w/v in 2% NaOH (w/v) aqueous solution) (RM-2) was added dropwise with constant stirring maintained under the nitrogen atmosphere. The resulting solution was further stirred for 3 h to allow complete Ostwald ripening (particle growth). The nickel nanoparticles were extracted by adding absolute ethanol to the reverse micellar solution containing Ni-nanoparticles followed by centrifugation at 3000–4000 rpm for 10 min. By varying the water content parameter W_0 (defined as the molar ratio of water to surfactant concentration, $W_0 = [\text{H}_2\text{O}]/[\text{surfactant}]$) the size of the nanoparticles could be controlled.

The sizes of the nickel-nanoparticles prepared at $W_0 = 5$ (the water content parameter W_0 can be defined as the ratio of molar concentration of water to surfactant, $W_0 = [\text{H}_2\text{O}]/[\text{surfactant}]$) were found to be as 15–18 nm through quasi elastic light scattering (QELS) data (Fig. 2a) and transmission electron microscopy (TEM) (Fig. 2b). The Ni-nanoparticles prepared were round in shape and black in color (colloidal state).

3.3. Typical procedure for the oxidative coupling of thiols

In a 50 ml round-bottomed flask a solution of thiol (2 mmol) in a solvent (20 ml) was prepared. nickel nanoparticles (15 mol%) were added to the solution and the reaction mixture was stirred at room temperature in air atmosphere.

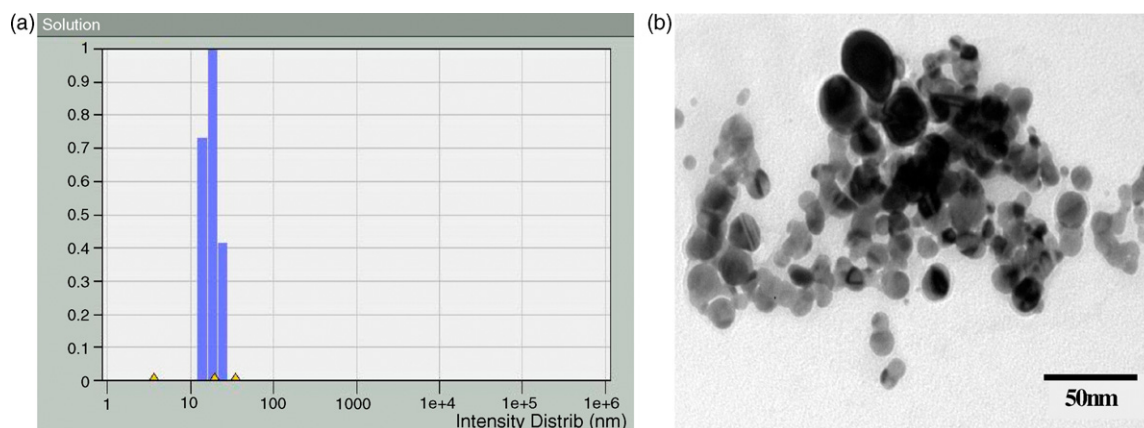


Fig. 2. (a) QELS data of Ni-nanoparticles: plot of population distribution in percentile vs. size distribution in nanometers and (b) TEM image of Ni-nanoparticles. The bar corresponds to 50 nm in the TEM.

The progress of the reaction was monitored by TLC (eluent: *n*-hexane/ethyl acetate, 4:1). The unreacted thiol was estimated by titrating against standard alcoholic iodine solution using pyridine as a base. After completion of the reaction, the reaction mixture was filtered and the solid material was washed with 10 ml of the same solvent used during the reaction. Excess solvent was evaporated using a rotatory evaporator and concentrating to dryness gave the desired product, which followed by recrystallization afforded the pure disulfides in 85–98% yields (Table 1). Comparison of the melting point/boiling point, ¹H NMR, ¹³C NMR, mass analysis and FT-IR spectra of the purified products with those of the authentic disulfides showed the purity of the disulfide products. All the authentic disulfides were prepared from the corresponding thiols according to the method described in Vogel [52]. Mass analysis and CHNS (elemental analysis) were done for some samples to check further oxidation of disulfides to disulfide sulfoxides (thiosulfinates), 1,1-dioxides (thiosulfonates) and sulfonic acids, which are quite possible. The analysis of complete spectral and compositional data revealed that only disulfides were formed and no further oxidation occurred.

3.4. Typical procedure for the recycling of the Ni-nanoparticles (catalyst)

After completion of the reaction, the reaction mixture was centrifuged at 2000–3000 rpm for 10 min which provided the catalyst Ni-nanoparticles as solid pellet at the bottom of the centrifuge tube. The nanoparticles were washed with CH₃CN 3–4 times to enforce the complete removal of any residual material. The particles were then re-dispersed in the desired solvent for further catalytic reaction cycle.

The same process was repeated after each reaction cycle to isolate and reuse the Ni-nanoparticles as catalyst.

4. Conclusion

Ni-nanoparticles (20 nm) act as green catalyst that can selectively catalyze oxidation of various thiols to disulfides and give no other side products. Further, our protocol avoids the use of expensive and harsh chemicals and high temperatures and leads to high yield of product in short reaction time under ambient conditions. The catalyst used in the reactions can be easily recovered.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.molcata.2006.12.042](https://doi.org/10.1016/j.molcata.2006.12.042).

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