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Oxidative dimerization of thiols to disulfide using recyclable magnetic nanoparticles

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Abstract Dimerization of thiol groups to disulfide is an important transformation in chemical processes. In this study, magnetic ion exchanged Montmorillonite-k10 was synthesized and characterized using FTIR, X-ray diffraction and scanning electron microscope techniques. Then, the application of the synthesized catalyst as an efficient oxidizing agent was evaluated in oxidative dimerization of different thiols to corresponding disulfides under optimal reaction conditions. The reaction was easily performed with aromatic, aliphatic and heterocyclic thiols. The magnetic catalyst was easily recovered by applying an external magnet and, further, was reused in successive reactions.

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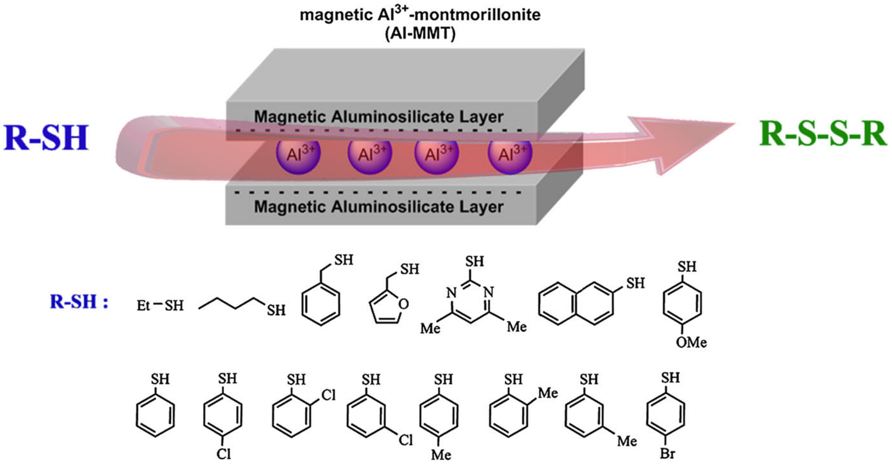
Graphical Abstract



Keywords Thiol · Disulfide · Cation exchanged Montmorillonite · Magnetic nanoparticles · Oxidative dimerization

Introduction

The conversion of thiols to the corresponding disulfides is an important reaction in chemical processes. Disulfides have industrial applications as vulcanizing agents [1] and are important synthetic intermediates with many applications in organic synthesis [2, 3]. Disulfide bond formation is important in peptides [4] and bioactive molecules [5]. Oxidative dimerization of thiols to disulfides under neutral and mild conditions without overoxidation is an important process in organic chemistry [6] and biochemistry [7], which has been investigated over the years. Many successful reagents have been developed for the synthesis of disulfides without over-oxidation of thiols to sulfoxides and sulfones [8]. Various reagents and oxidants have been employed for the conversion of thiols to disulfides. This conversion has been accomplished using reagents such as permanganates [9], sodium perborate [10], ferric chloride [11], sodium chlorite [12], hydrogen peroxide [13], halogens [14], molecular oxygen [15], PCC [16], ammonium persulfate [17], 2,6-dicarboxypyridinium chlorochromate [18], 1,3-dibromo-5,5-dimethylhydantoin [19], *N*-phenyltriazolinedione [20], molecular bromine on hydrated silica gel support [21], iodine and $CeCl_3{\cdot}7H_2O$ in graphite [22], monochloro poly(styrenehydantoin) beads [23], solid anhydrous potassium phosphate [24], cetyltrimethylammonium dichromate [25], sulfuryl chloride [26], benzyltriphenylphosphonium peroxymonosulfate [27], silica-supported bis (trimethylsilyl) chromate [28], selenium ionic liquid [29], and in the absence of any catalyst [30–32].

Clays function as efficient catalysts for various organic transformations due to their catalytic activities in both their natural and ion-exchanged forms [33].

Commercially available Montmorillonite K-10 (MMT) is environmentally benign and an economically feasible solid catalyst that offers several advantages, such as operational simplicity, non-corrosiveness, non-toxicity, low cost, easy isolation and reusability [34]. Its high surface area (250 m^2/g) make it a useful and active catalyst. Due to its structural features and synthetic potential, MMT has been used extensively as a strong catalyst in organic synthesis [35] and has been emerging as a very convenient support for a series of synthetic transformations.

Here, we extended our previous experience on solid supported reactions [36]. In the course of studies on some reactions of MMT, we observed the oxidative dimerization of thiols. In this study, we synthesized magnetically recoverable cation-exchanged Al^{3+}-Montmorillonite (Al-MMT) as an efficient catalyst (Fig. 1). We have employed a simple, fast, and one-pot procedure with a simple workup for efficient dimerization of a variety of thiols to their corresponding symmetrical disulfides on Al-MMT without any reagents. A set of experiments were performed to find the best conditions for the oxidation, using thiophenol as a model compound.

Experimental

Materials and methods

All the products were characterized by comparing their physical and spectral data with those of known samples. All yields refer to isolated products. TLC experiments were carried out on silica gel plates with a UV indicator from Aldrich, visualization was by UV fluorescence or by staining with iodine vapor. IR spectra were recorded on a Bruker Vector 22 FT-IR spectrophotometer using KBr disks or as neat samples. The morphology of the catalytic particles was checked employing a scanning electron microscope (AIS2300C SEI) at an accelerating voltage of 20 kV. The X-ray diffraction (XRD) patterns were reported with a Philips X'Pert MPD diffractometer equipped with Cu Kα radiation ($\lambda = 0.154$ nm) in the range 10°–80° (2θ) at a speed of 0.05°/min. Montmorillonite K-10 (MMT) having a surface area 250 m^2/g was purchased from Aldrich Chemical. All chemicals were also available from Aldrich and used as purchased.

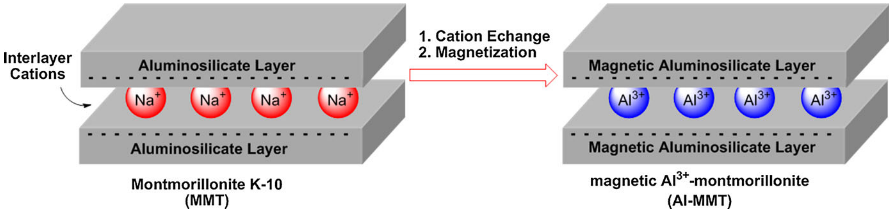


Fig. 1 Synthesis of magnetic Al^{3+}-Montmorillonite (Al-MMT)

Catalyst preparation

Cation-exchanged MMT was synthesized and analyzed according to the literature [37]. MMT (5.00 g) was added gradually to a solution of aluminum nitrate (0.3 M, 80 ml) in a 250-ml flask equipped with a condenser and mechanical agitator, and stirred for 4 h at room temperature. Then, the solid precipitate was filtered, washed with water (2 ml × 80 ml) and dried in a vacuum oven for 2 h at 100 °C. Finally, it was calcinated in an oven for 3 h at 300 °C to obtain Al-MMT.

The co-precipitation method was performed for the magnification of cation-exchanged MMT using ultrasonic waves. Al-MMT (5.0 g), $FeCl_2 \cdot 4H_2O$ (9.94 g, 50 mmol,) and $FeCl_3 \cdot 6H_2O$ (0.27 g, 100 mmol) were added to distilled water (100 ml) in a 250-ml flask equipped with a condenser and mechanical agitator under nitrogen gas flow, and stirred for 30 min. Then, a concentrated ammonia solution (3.5 M) was added dropwise within 1 h under ultrasonic irradiation and refluxed for 1 h at 80 °C. After cooling, the magnetic precipitate was isolated from the reaction mixture with a strong magnet, washed with water (5 ml × 100 ml) and was at 80 °C in an oven for 12 h to obtain Al-MMT. The SEM images and FT-IR spectra of MMT and Al-MMT are displayed in Figs. 2 and 3.

The X-ray diffraction patterns of Al-MMT are shown in Fig. 4. The XRD spectra show that amorphous silica is the most dominant peak.

Optimization of synthesis conditions using catalysts

After synthesis and characterization of the magnetic catalyst, its effect on oxidative dimerization of thiols was examined. A homogeneous mixture of thiophenol (0.55 g, 5 mmol) and Al-MMT (1.0 g) in tetrahydrofuran (10 ml) as a solvent was stirred at 50 °C for 2 h (Table 1). The progress of the reaction was monitored by TLC until complete disappearance of the starting material. After completion of the reaction, the mixture was cooled to room temperature. The catalyst system was removed from the reaction mixture with a strong external magnet, washed with ethanol (10 ml) and diethyl ether (10 ml) and dried in an oven. Tetrahydrofuran was concentrated under vacuum to yield the corresponding disulfide (1.05 g, 96 %). If necessary, the product was further purified by column chromatography over silica

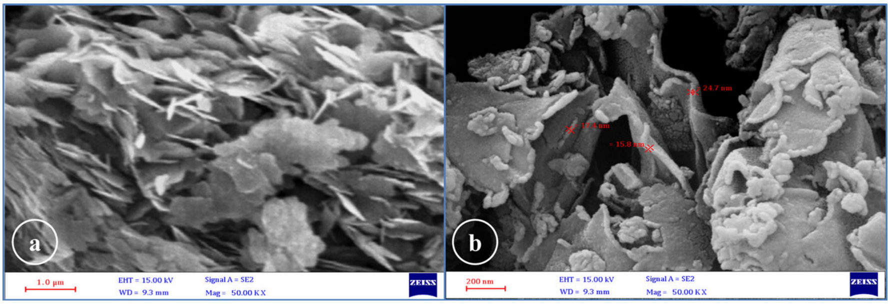


Fig. 2 SEM images of **a** MMT and **b** Al-MMT

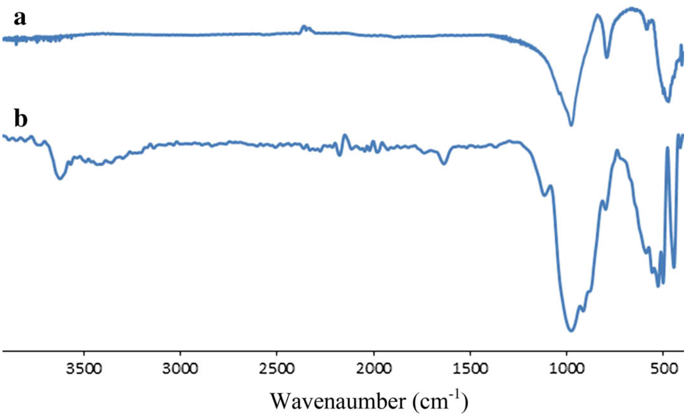


Fig. 3 FT-IR spectra of *a* MMT and *b* Al-MMT

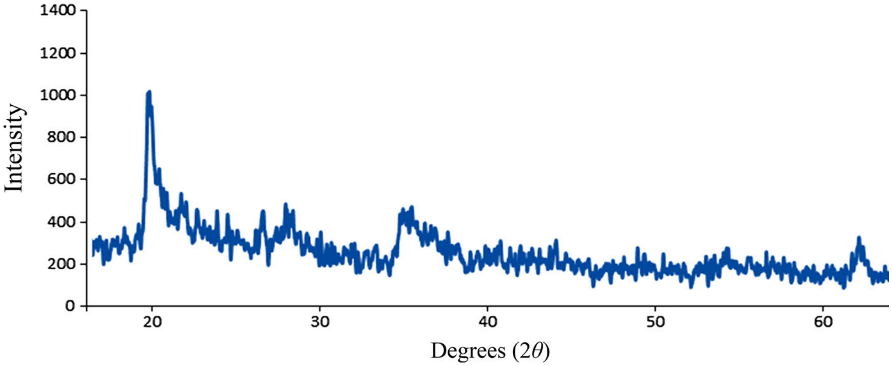


Fig. 4 XRD pattern of Al-MMT

Table 1 Oxidative dimerization of thiophenol with different catalysts[a]

Entry	Catalyst	Solvent	Time (min)	Yield (%)[b]
1	MMT	Dichloromethane	120	71
2	Al-MMT	Dichloromethane	120	88
3	Al-MMT	Acetonitrile	120	83
4	Al-MMT	Diethyl ether	120	85
5	Al-MMT	Ethanol	120	5
6	Al-MMT	Toluene	120	34
7	Al-MMT	Acetone	120	75
8	Al-MMT	Ethyl acetate	120	80
9	Al-MMT	Tetrahydrofurane	120	96
10	Al-MMT	Tetrahydrofurane	120	63[c]
11	Al-MMT	Tetrahydrofurane	60	90

[a] Reactions conditions: thiophenol (5 mmol, 0.55 g), catalyst (0.1 g), solvent (10 ml), 50 °C

[b] Isolated yield

[c] The reaction was performed at room temperature

gel (eluent: hexane/dichloromethane) or by bulb to bulb distillation. The above-mentioned oxidation procedure for thiophenol is representative of all thiols presented in Table 2.

Results and discussion

In this study, the cation exchange process in MMT resulted in increased acidity. As a result, the reaction yields were increased (Table 1). Electron transfer between the aluminum ions existing between MMT layers can activate the thiol functionality to oxidative dimerization of sulfurs (Fig. 5). The difference between MMT and Al-MMT was identified by investigating more reactions. Al-MMT as a Lewis acid can act as a promising alternative for the Brønsted acids as an acid catalyst.

To complement the findings, a series of different thiols were employed in this study, and the results are presented in Table 2. The results of the oxidation reactions of these thiols presented in Table 2 indicate that the present method is equally applicable for the oxidative coupling of alkyl thiols (Table 2, entries 1, 2), aryl thiols (Table 2, entries 3–14), and heterocyclic thiols (Table 2, entries 15, 16). Excellent results in thiol dimerization to disulfides was observed, except for 2-thionaphthol, which was probably due to steric hindrance caused by the bulky naphthyl group (Table 2, entry 11). The reactions were carried out under mild conditions with excellent yields and simple workup. A simple separation of the magnetic catalyst with an external magnet at the end of the reaction, followed by removal of the solvent under reduced pressure from the filtrate, allows product isolation. Impure products were purified utilizing column chromatography. Methyl, methoxy, benzylic, carboxyl and halogen functionalities did not interfere with the oxidation of the thiol group. As expected, sterically hindered thiols have slightly lower yields compared to sterically unhindered thiols. High yields and high purity in most cases were indicated by the TLC analysis and melting point compared with those reported in the literature.

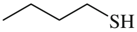
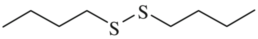
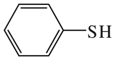
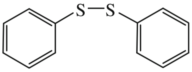
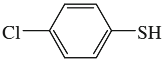
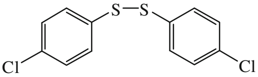
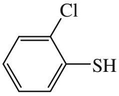
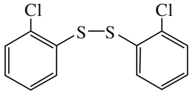
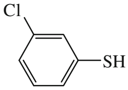
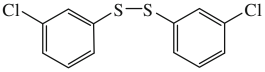
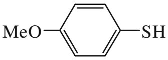
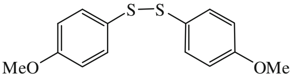
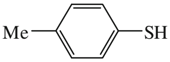
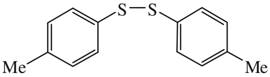
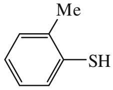
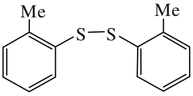
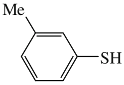
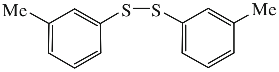
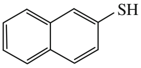
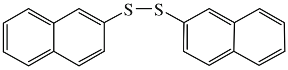
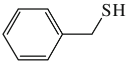
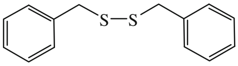
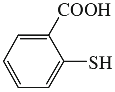
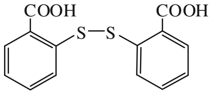
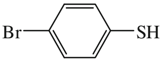
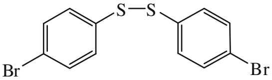
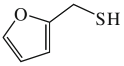
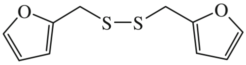
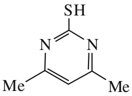
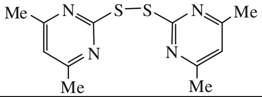
The FT-IR spectra were evaluated to analyze the functional groups of the thiophenol and diphenyl disulfide (Fig. 6). The FT-IR spectrum shows that the thiophenol was almost completely dimerized to diphenyl disulfide, so that the S–H peak in thiophenol (Fig. 6a) was not observed in the product (Fig. 6b). EI Mass spectrum of diphenyl disulfide is also shown in Fig. 7.

Reusability of catalyst

The reusability of Al-MMT was investigated in the oxidative dimerization of thiophenol as a model. At the end of the reaction, Al-MMT was separated using an external magnet, washed with dichloromethane and dried at 50 °C for 6 h. After magnetic separation and product workup, the catalyst was reused for five successive reactions, and the catalytic performance remained almost constant without any remarkable decrease in catalytic activity (Fig. 8).

Table 2 Oxidative dimerization of thiols to disulfide with Al-MMT as catalyst[a]

$$\textbf{R-SH} \xrightarrow{\text{Al-MMT / THF / 50 °C}} \textbf{R-S-S-R}$$

Entry	Thiol	Product	Time (min)	Yield (%)[b]	m.p. (°C)	References
1	Et-SH	Et-S-S-H	60	88	Oil	[28]
2			60	91	Oil	[28]
3			60	96	59–60	[22]
4			60	95	73–74	[18]
5			60	83	67–69	[29]
6			60	90	81–82	[10]
7			60	92	43–44	[29]
8			80	86	41–43	[29]
9			60	72	36–38	[28]
10			60	80	54–57	[29]
11			120	65	138–140	[29]
12			90	90	70–71	[29]
13			60	68	288–290	[18]
14			60	95	94–95	[18]
15			90	77	81–85	[36]
16			90	78	168–170	[22]

[a] Reactions conditions: thiole (5 mmol), catalyst (0.1 g), Tetrahydrofuran (10 ml), 50 °C

[b] Isolated yield

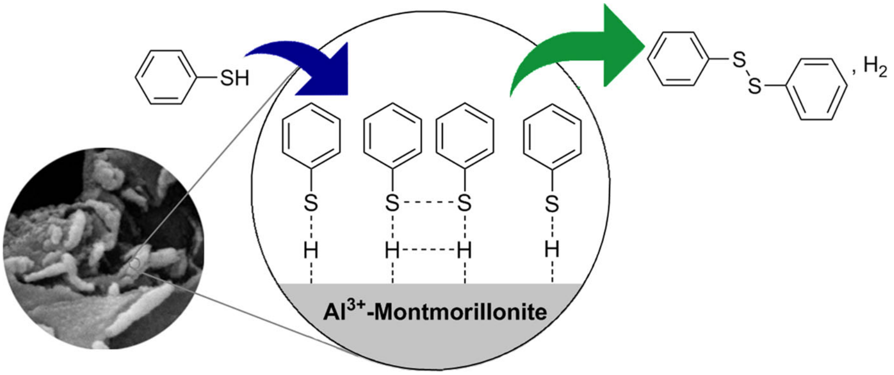


Fig. 5 Oxidative dimerization of thiophenol using Al-MMT

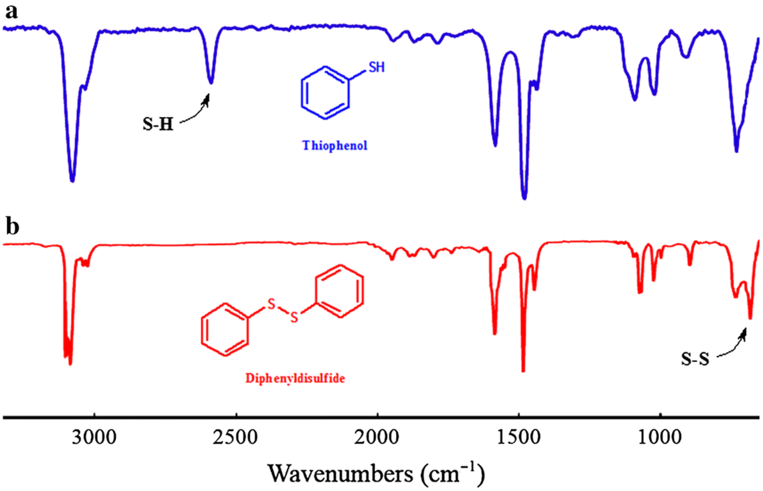


Fig. 6 FT-IR spectra of *a* thiophenol and *b* diphenyldisulfide

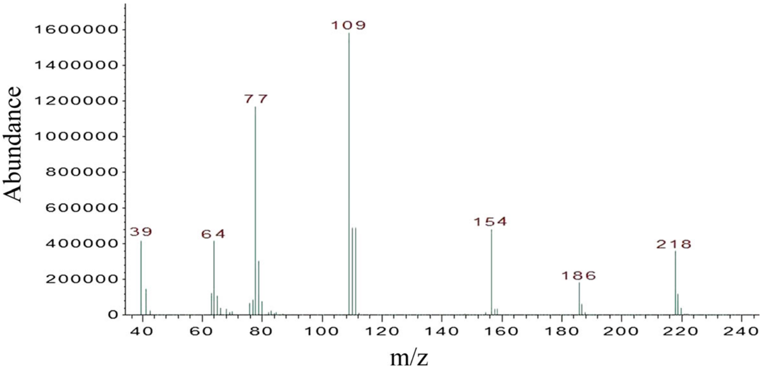


Fig. 7 EI Mass spectrum of diphenyldisulfide

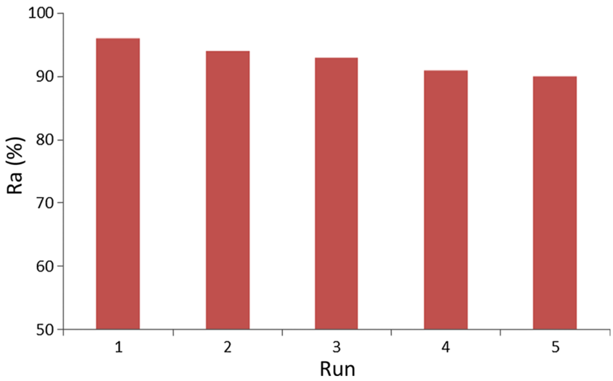


Fig. 8 Recyclability of the catalyst Al-MMT in the oxidative dimerization of thiophenol

Conclusion

Cation-exchanged Montmorillonite (Al-MMT) has been used as a catalyst for many organic reactions and has several advantages compared to conventional acids, such as strong acidity, non-corrosive properties, mild reaction conditions, high yields and selectivity. On the other hand, the magnetic property of magnetic nanoparticles in the catalytic support facilitates the separation and recycling of the catalyst of the reaction medium, more easily than filtration or centrifugation.

In conclusion, the method for oxidizing aliphatic, aromatic, and heteroaromatic thiols with Al-MMT, as reported in this paper, is a simple, fast, efficient, inexpensive, easy to handle, very mild procedure. In this study, we have developed a mild, efficient and good yielding method for the oxidation of thiols. In addition, rapid completion of the reactions, environmental safety of the process, high yields of the products, simple separation of the magnetic catalyst, clean workup and excellent purity of products are worthwihle advantages of the present method that makes it an attractive and useful procedure for the oxidation of thiols to corresponding disulfide compounds. Moreover, the method is applicable to a wide variety of thiols, being a useful alternative to other methods in the literature.

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