



AN EFFICIENT CONVERSION OF EPOXIDES TO THIIRANES WITH THIOUREA CATALYZED BY NANO CRYSTALLINE $\text{SnO}_2/\text{Al}_2\text{O}_3$

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Abstract- A heterogenous catalyst nano crystalline SnO_2 dispersed on amorphous alumina was prepared by simple hydrothermal method. This catalyst was employed for one-pot conversion of epoxides to thiiranes. in good to excellent yields. The catalyst was recovered quantitatively by simple filtration and reused several times with almost consistent activity.

Key words: Nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$; hydrothermal; thiiranes; epoxides; heterogeneous catalyst.

1. Introduction

Thiiranes [i-iv] play an increasing pivotal role in organic synthesis as versatile building blocks in asymmetric reactions. Moreover, they have wide range of industrial applications as disinfectants, as precursors for synthetic polymers[v], as stabilizers for plastics, and as pharmacologically active substances. For example, *S*-thiirane carboxylic acids and thiodiols are used as selective inhibitors for cysteine protease, and cancer therapy respectively. The successful use of thiiranes in industry and biology stimulated various authors to investigate the chemistry of this group of compounds in more detail. Knapp et al. reported the utility of thiirane intermediates in the synthesis of thioglycosides [vi]. Their oxygen analogs, epoxides, have enjoyed numerous synthetic applications due in part to their relative ease of handling, and reactivity with a range of nucleophiles with predictable regio and stereoselectivity. Thiiranes offer these synthetic possibilities combined with the rich chemistry that a vicinal thiol group in the product provides. Extensive development of this chemistry of thiiranes has been thwarted in part by the observation that yields of nucleophilic substitution products can be significantly lowered by polymerization side reactions occasioned by the generation of nucleophilic products that compete for unreacted thiirane. In addition, certain physical properties of low molecular weight sulfur compounds have diminished their attractiveness to potential practitioners [vii]. Nucleophilic ring-opening of thiiranes serves as a convenient access to sulfur-containing compounds, which include thiols, thioethers, cyclic sulfides, sulfoxides, sulfones, sulfinates, sulfonates, etc[viii]. Moreover, episulfides have been employed in numerous commercial and industrial applications, in particular as disinfectants [ix], as precursors for synthetic polymers [x], as stabilizers for plastics [xi], and as pharmacologically

active substances [xii-xiii]. In view of the practical need and synthetic utility, it is highly desirable to have available convenient methods for the preparation of episulfides.

Several methods have been developed for the synthesis of thiiranes which have been extensively reviewed [14,15,16]. Recently, special catalysts have been used for the transformation of oxiranes into thiiranes under mild conditions to afford thiiranes in good yields [xvii- xxi]. A number of methods using aluminum tris (dodecyl sulfate) trihydrate $\text{Al}(\text{DS})_3 \cdot 3\text{H}_2\text{O}$ as a Lewis acid–surfactant [xxii], $\text{HBF}_4\text{-SiO}_2$ [xxiii], polyethylene glycol (PEG-400) [xxiv], cyanuric chloride [xxv], $\text{Bi}(\text{TFA})_3/\text{Bi}(\text{OTf})_3$ [xxvi] have been reported. Conversion of epoxides to thiiranes was also performed efficiently in the presence tin(IV) meso-tetraphenylporphyrin $[\text{Sn}(\text{IV})(\text{tpp})(\text{ClO}_4)_2]$ [xxvii] and tin(IV)tetraphenylporphyrinato tetrafluoroborate $[\text{Sn}^{\text{IV}}(\text{tpp})(\text{BF}_4)_2]$ [xxviii], LiBF_4 [xxix], SiCl_4 [30], silica gel–supported AlCl_3 [xxx], TiO_2 [xxxii], β -cyclodextrin [xxxiii]. The most common sulfur introducing reagents in the synthesis of thiiranes are thiocyanates and thiourea. In recent years, emphasis is on the use and design of environmentally friendly solid catalysts to reduce the amount of toxic waste. Nanomaterials are of topical interest as there are many reports in the literature on the synthesis of transition metal nano particles and their application as catalysts. The synthesis of nano crystalline SnO_2 dispersed on amorphous alumina was carried out by a simple hydrothermal method using simple salt precursors with urea as the hydrolytic agent [xxxiv]. In the present work, the nano crystalline SnO_2 dispersed on alumina was prepared by simple hydrothermal method is applied for one-pot synthesis of thiiranes. The methodology for the synthesis of thiiranes from oxiranes is by an oxygen-sulfur exchange reaction. The nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$ catalyst samples with various Sn:Al ratios, solvents and ring opening sulfur reagents has been explored. The catalyst is recovered by simple filtration and reused for several cycles with consistent activity in good yields.

2. Results and discussion

EDAX analysis of the as prepared $\text{SnO}_2/\text{Al}_2\text{O}_3$ showed the following elemental composition: Sn, 35.82; O, 50.62; Al, 11.21; Cl, 2.36. The ratio of Sn:Al (1:1) in the as prepared sample concur with the molar ratios taken in the hydrothermal solutions. The diffraction patterns of $\text{SnO}_2/\text{Al}_2\text{O}_3(1:1)$ samples as prepared are shown in **Figure 1**. All the peaks can be indexed to that of tetragonal SnO_2 (JCPDS No. 21-1250). Alumina in $\text{SnO}_2/\text{Al}_2\text{O}_3$ mixed oxide exists in the amorphous phase. The SEM and TEM images of $\text{SnO}_2/\text{Al}_2\text{O}_3(1:1)$ in as prepared sample are shown in **Figure 2**. TEM images show the amorphous phase of boehmite in the as-prepared sample having nanometric particles. Boehmite particles exist as porous agglomerates of irregular size and shape overlapping each other with pores in between while the SnO_2 could be seen as fine spindle like structures distributed at random and placed mostly on the surface of AlOOH agglomerates. This sample shows two types of particles in the nanometric scale: spherical shaped dark particles in the range of 20-50 nm that appears to have a random distribution; a cloud of nanometric particles of about 2 nm touching each other with free spaces so that the mass looks very porous. They show a very broad size distribution with no faceted aggregates.

The catalytic property of nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$ was investigated for the oxygen-sulfur exchange reaction between oxiranes and ring opening sulfur-reagents (thiocyanates/thiourea) (**Scheme 1**). Initially, the effect of catalyst was examined for the reaction between styrene epoxide and thiourea in acetonitrile with different nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$ samples at room temperature as well as reflux temperature and the results are presented in **Table 1**. As prepared nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$ with 1:1 ratio is found to be the best catalyst for obtaining high yields. While under similar conditions a blank experiment in acetonitrile after 8 h provided no product (**Table 1, entry 7**) and with nano- SnO_2 , 73% product was isolated after 1 h (**Table 1, entry 6**). The products were quantitatively recovered by simple filtration and extraction with ethyl acetate.

Then, the effect of various solvents and sulfur introducing reagents for the conversion of styrene epoxide into corresponding thiirane with nano-SnO₂/Al₂O₃ (Sn:Al = 1:1) at room temperature are examined and the results are presented in **Table 2**. Acetonitrile and thiourea are found to be the best solvent sulfur donating reagent respectively for obtaining high yields. A variety of oxiranes were subjected to the exchange reaction with thiourea using nano-SnO₂/Al₂O₃. The reaction of styrene epoxide and thiourea in acetonitrile after 0.5 h with 10 mol% of the catalyst resulted in 98% of product. Then we applied similar reaction conditions for the preparation of structurally diverse thiiranes from different epoxides in order to show the general applicability of the method. Different types of oxiranes such as styrene oxides, aromatic and bicyclic oxiranes including those with electron-withdrawing and electron-donating substituents, underwent smooth conversion into thiiranes. The results are summarized in **Table -3**. The products were formed in excellent yields and no side products were detected. The reactions proceeded smoothly and efficiently in this optimized reaction condition with excellent isolated yields in short reaction time.

3. Experimental

3.1. Materials

Epoxides were purchased from Aldrich or Fluka and thiourea, SnCl₂.2H₂O, Al(NO₃)₃.9H₂O were purchased from SD Fine chemicals. All chemicals are used without further purification. ACME silica gel (60–120 mesh) was used for column chromatography and thin-layer chromatography was performed on Merck-precoated silica gel 60-F254 plates. All the other solvents and chemicals were obtained from commercial sources and purified using standard methods.

3.2. Catalyst preparation

The reactants for the system were SnCl₂.2H₂O (0.05mol, 11.28 g) and Al(NO₃)₃.9H₂O (0.05 mol, 18.75 g); they were dissolved in 250 ml of water and then, urea (0.4 mol, 24 g) was added to the homogeneous mixture and this hydrothermal solution was transferred to an autoclave. The temperature was allowed to reach to 180°C within an hour (ramp time). The reaction was kept at this temperature for 2 hours (soak time) with an in-situ pressure of 12 atm. After 2 hours, it was cooled down to room temperature. The product was filtered, washed with water and dried at 110°C in a hot air oven. The initial pH of the hydrothermal solution was acidic (pH 4) and the final pH was alkaline (pH 8.5). Finally, the dried powders were calcined at 600, 1000 and 1200°C in a muffle furnace for 3 hours. A similar procedure was followed for the preparation of 1:2 and 2:1 nano-SnO₂/Al₂O₃ samples.

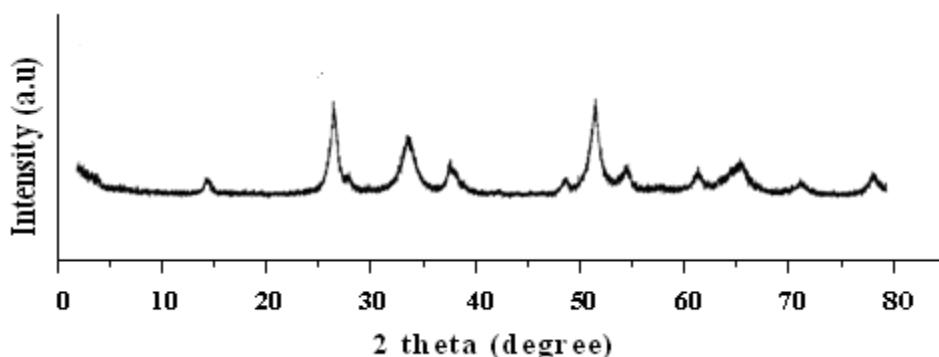


Figure 1. XRD pattern of as prepared nano-SnO₂/Al₂O₃

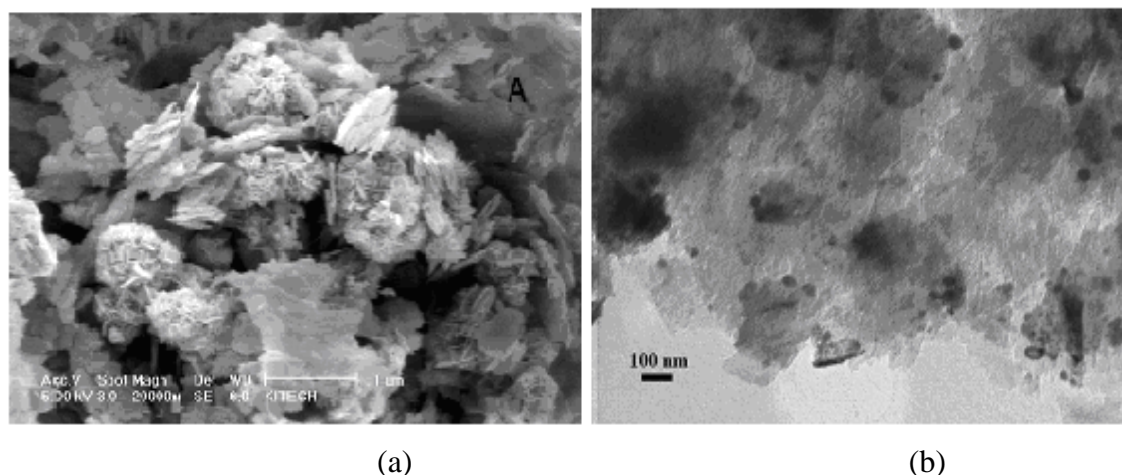


Figure 2. (a)SEM and (b)TEM images of as prepared $\text{SnO}_2/\text{Al}_2\text{O}_3$ by hydrothermal method.

3.3. Typical experimental procedure for the synthesis of thiiranes

Nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$ (10 mol%) was added to a mixture of oxirane (1 mmol), thiourea (2 mmol) in acetonitrile (4 mL) and stirred at room temperature for 0.5 h. After completion of the reaction (as monitored by TLC), the catalyst was separated by simple filtration and the resulting mixture was extracted with ethyl acetate (5 mL). The organic phase was separated and dried over anhydrous Na_2SO_4 , and concentrated to give crude desired product. Purification of the crude product was performed by column chromatography on silica gel eluted with ethyl acetate in n-hexane (1:9) to afford the pure product in excellent yields. All the products were analyzed by ^1H NMR spectra, mass spectra and CHNS elemental analysis. Spectral data for selected compounds follow.

Table 1. Effect of catalyst on the synthesis of thiiranes using nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$.^a

Entry	Catalyst	Time (hrs)	Isolated Yield (%) ^b
1	$\text{SnO}_2\text{-Al}_2\text{O}_3$ (1:1)	0.5	97, 98 ^c
2	$\text{SnO}_2\text{-Al}_2\text{O}_3$ (2:1)	0.5	89
3	$\text{SnO}_2\text{-Al}_2\text{O}_3$ (1:2)	0.5	62
4	AlOOH	2	No reaction
5	$\text{SnO}_2\text{-Al}_2\text{O}_3$ (1:1) Calcined at 600°C	2	84
6	SnO_2	1	73
7	No Catalyst	8	No reaction

Reaction conditions: Styrene epoxide (1 mmol), thiourea (2 mmol) in 4mL acetonitrile, 10 mol% nano- $\text{SnO}_2/\text{Al}_2\text{O}_3$ and room temperature.

^b Yields of isolated products. ^c Reflux temperature

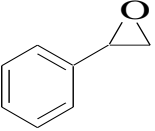
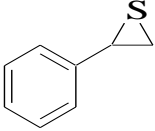
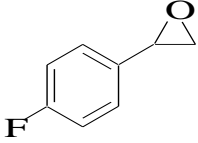
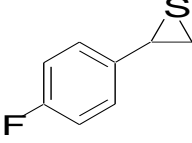
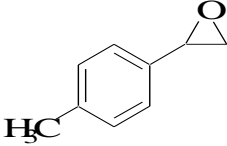
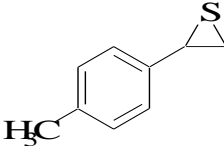
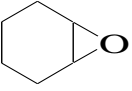
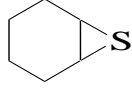
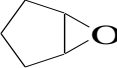
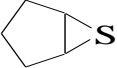
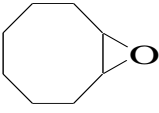
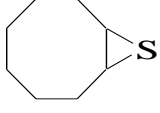

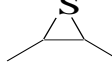
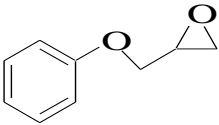
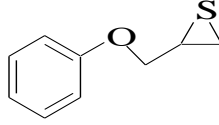
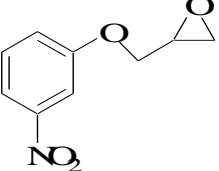
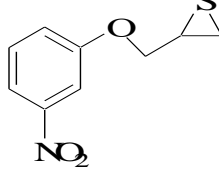
Table 2. Effect of catalyst on the synthesis of thiiranes using nano-SnO₂/Al₂O₃^a.

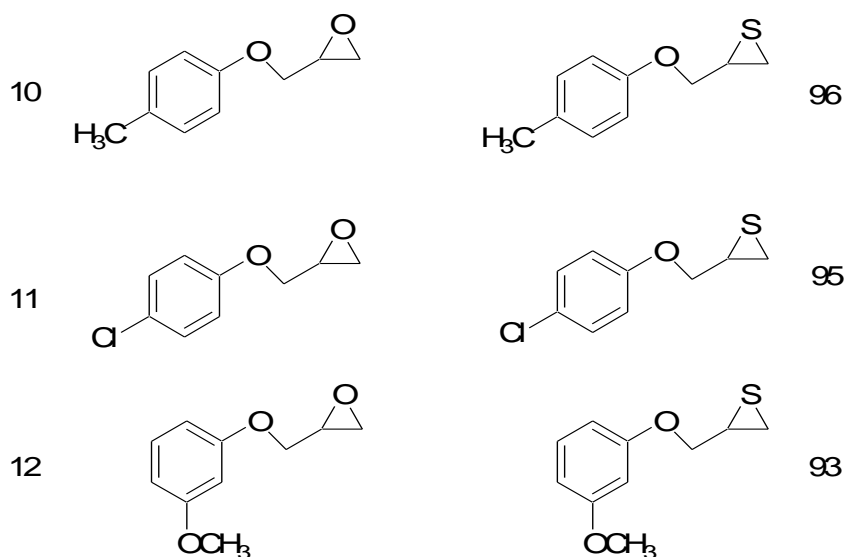
Entry	Solvent	Temperature	Sulfur introducing reagent	Isolated Yield (%) ^b
1	H ₂ O	RT	tu	No reaction
2	H ₂ O	RT	NaSCN	No reaction
3	CH ₃ CN	RT	tu	97
4	CH ₃ CN+ H ₂ O	RT	tu	63
5	AcOH	RT	tu	84
6	CH ₃ CN	Reflux	NaSCN	86
7	CH ₃ CN	Reflux	NH ₄ SCN	73

^aReaction conditions: styrene epoxide (1 mmol), Sulfur introducing reagent (2 mmol) in 4mL acetonitrile, 10 mol% nano-SnO₂/Al₂O₃.

^b Yields of isolated products.

Table 3. Synthesis of thiiranes from epoxides using nano-SnO₂/Al₂O₃^a

Entry	Epoxide	Thiirane	Yield(%) ^b
1			98, 97 ^c
2			95
3			97
4			98
5			97
6			98
7			94
8			96
9			92



^aReaction conditions: oxirane (1 mmol), thiourea (2 mmol), 10 mol% nano-SnO₂/Al₂O₃, reaction time 0.5 hrs and room temperature.

^b Yields of isolated products.

^c Yield after fourth cycle.

4. Recyclability

The heterogeneity of the nano-SnO₂/Al₂O₃ was evaluated by the following studies. The nano-SnO₂/Al₂O₃ catalyst was removed after the reaction by centrifugation, fresh aliquots of reactants were added to the centrifuged solvent and the reaction was monitored. The formation of the desired product was not observed indicating that there is no leaching of the catalyst. Further, the recovered catalyst was reused for four cycles with consistent activity in the synthesis of thiiranes and the results are presented in **Table 2, entry 1c** for the selected substrate. The catalyst displayed good recyclability. The tin content was found to be almost same in the fresh and used catalyst after the fourth cycle as shown by ICP-AES analysis. These studies demonstrate that the nano-SnO₂/Al₂O₃ during the reaction is active and the reaction proceeds on the heterogeneous surface.

Spectral data of new thiiranes

2-Phenyl thiirane(**Table 3, Entry 1**)¹H NMR (300 MHz, CDCl₃): δ = 7.15-7.30 (5H, m), 3.58 (1H, t, *J*=6.2 Hz), 2.8 (1H, dd, *J*=6.2, 1.8 Hz), 2.55 (1H, dd, *J*=6.2, 1.8 Hz); MS: *m/z* =136 [M]⁺; Anal. Calcd for C₈H₈S: C, 70.58; H, 5.88; S, 23.53 %; Found : C, 70.66 H, 5.93; S, 23.60 %.

Cyclohexane thiirane:(**Table 3, Entry 4**)¹H NMR (300 MHz, CDCl₃): δ =1.10–1.46 (m, 4 H), 1.60–1.80(m, 2H), 2.0–2.20 (m, 2H), 2.91 (m, 2H); MS: *m/z* 114 [M]⁺;Anal. Calcd for C₆H₁₀S: C, 63.15; H, 8.77; S, 28.07 %; Found: C, 63.23; H, 8.64; S, 28.18 %.

2-phenoxyethyl thiirane (**Table 3, Entry 8**)¹H NMR(300 MHz, CDCl₃): δ= 2.33 (dd, 1H, *J* = 4.3 and 6.4 Hz), 2.61 (dd, 1H, *J* = 4.3 and 5.0 Hz), 3.28 (m, 1 H), 4.2 (d, 2H, *J* = 6 Hz), 7.25–7.48 (m, 5 H); MS: *m/z* 166 [M]⁺;Anal. Calcd for C₉H₁₀OS: C, 65.06; H, 6.02; S, 19.28 %; Found: C, 65.30; H, 6.18; S, 19.30 %.

2-(4-Tolylloxymethyl) thiirane (**Table 3, Entry 10**) ¹H NMR (300 MHz, CDCl₃): δ = 7.18 (2H, d, *J* = 8.0 Hz), 6.80 (2H, d, *J* = 8.0 Hz), 4.41 (1H, dd, *J* = 6.2, 1.8 Hz), 3.78 (1H, dd, *J* = 6.2, 1.8 Hz), 3.28 (1H, m), 2.50 (1H, dd, *J* = 6.0, 1.8 Hz), 2.29 (1H, dd, *J* = 6.0, 1.8 Hz) 2.28 (3H, s); MS: *m/z* = 181 [M+H]⁺; Anal. Calcd for C₁₀H₁₂OS: C, 66.66; H, 6.66; S, 19.28 %; Found: C, 66.75; H, 6.18; S, 19.10 %.

2-(4-Chloro phenoxy)methyl) thiirane (Table 3, Entry 11)¹H NMR (300 MHz, CDCl₃): δ = 7.31 (2H, d, *J* = 8.0 Hz), 6.9 (2H, d, *J* = 8.0 Hz), 4.30 (1H, dd, *J*=6.5, 1.7 Hz), 3.85 (1H, dd, *J*=6.5, 1.7 Hz), 3.23 (1H, m), 2.60 (1H, dd, *J*=6.1, 1.8 Hz), 2.30 (1H, dd, *J*=6.1, 1.8 Hz); MS: *m/z* = 200 [M]⁺; Anal. Calcd for C₉H₉OSCl: C, 53.86; H, 4.48; S, 19.28 %; Found: C, 53.93; H, 4.68; S, 19.27%.

5. Conclusions

In conclusion, nano-SnO₂/Al₂O₃ was prepared by simple hydrothermal method and employed for the conversion of epoxides to thiiranes with thiourea with a variety of substrates which afford excellent yields. The catalyst was recovered by simple filtration and reused for several cycles.

6. Conflict of interest: Author has no conflict of interest.

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