A green protocol for rapid and efficient conversion of epoxides to thiiranes using alumina immobilized thiourea at solvent-free conditions

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ABSTRACT
Solvent-free conversion of various epoxides to the corresponding thiiranes was carried out successfully with alumina-immobilized thiourea at room temperature. The reactions were completed within 2–9 min to give thiiranes with 83–98% yields. The utilized alumina can be reused for several times without losing its activity.

GRAPHICAL ABSTRACT

R, R’ : aryl, alkyl, allyl, H

Introduction
Thiiranes, the simplest sulfur heterocycles, play an increasing pivotal role in organic synthesis as versatile building blocks in asymmetric reactions. Moreover, they are used as intermediates in the pharmaceutical, polymer, pesticide, and herbicide industries. The literature review shows that thiiranes are prepared by various methods. Thiourea, dimethylthioformamide, inorganic thiocyanates, polymer supported thiocyanate, and silica supported potassium thiocyanate have been used as sulfur transferring agents for the conversion of epoxides to thiiranes. The combination systems of different Lewis acids or reagents such as zeolite molecular sieve 4Å, CaCO₃, InBr₃, TiO₂, Bi(TFA)₃, Mg(II)₃, Al(DS)₃, HClO₄, LiClO₄, SiO₂·HBF₄, oxalic acid, montmorillonite K₁₀, LiBF₄, 2,4,6-trichloro-1,3,5-triazine, (NH₄)₆[CeW₁₀O₃₆]·20H₂O, [bmim]PF₆, β-cyclodextrin, polyestryne supported AlCl₃, polymeric co-solvents, Sn(TTP)-(OTf)₂, Sn(TTP)(BF₄)₂, etidronic acid, NH₄Cl, Dowex-50WX₈, and microwave irradiation with thiourea or ammonium thiocyanate have been used for the preparation of thiiranes from epoxides. Recently, the successful use of ammonium thiocyanate under catalyst- and solvent-free condition at 60–90°C as well as sodium thiocyanate/graphite oxide has been documented for the titled transformation. Although, most of the mentioned methodologies are useful for the preparation of thiiranes from epoxides, some of them suffer from disadvantages such as long reaction times, high temperature reaction conditions, use of volatile and toxic solvents, poor yields, formation of several by-products and the use of foul smelling reagents which must be handled with care.

In recent years, the use of reagents and catalysts immobilized on solid supports has received considerable attention. Such reagents not only simplify purification processes, but also help to prevent the release of reaction residues into the environment. In the light of emerging new solid supported reagents as efficient and recyclable catalysts/promoters, herein we wish to report a green, efficient and practical approach for the synthesis of thiiranes from epoxides using alumina immobilized thiourea as an eco-friendly reagent at room temperature and under solvent-free condition (Scheme 1).

Results and discussion
In organic synthesis and reactions, increasing attention is being focused on green chemistry, particularly solvent-free procedures by grinding under heterogeneous conditions. Solvent-free procedures are facilitated by supported reagents on various solid inorganic surfaces, and often lead to clean, low cost, eco-friendly, and highly efficient procedures involving simplified and easy workups. In the course of our interests to use green protocols for the preparation of thiiranes from epoxides, we found that alumina immobilized thiourea as an easily available reagent promotes the conversion of epoxides to the corresponding thiiranes at solvent-free conditions.
The optimized experimental conditions showed that the reaction of styrene oxide (1 mmol) with thiourea (2 mmol) immobilized on alumina (0.6 g) can be carried out efficiently at room temperature and under solvent-free condition by grinding (Table 1, entry 4). The epoxide was completely converted to the corresponding thiirane within 3 min. Initially, we carried out the titled reaction with different amounts of alumina at room temperature and under solvent-free condition. It was found that the best result was obtained with 0.6 g alumina. It is notable that in the absence of alumina, the reaction did not at all take place even after a prolonged reaction time. Moreover, the effect of solvents such as CH$_3$CN, n-hexane, EtOAc, THF, EtOH, and acetone was investigated for the typical experiment under reflux conditions. The results showed that the rate enhancement and efficiency at solvent-free conditions was higher than the solution phase (Table 1).

The green aspect of this synthetic method was investigated by recovering of alumina from the reaction mixture and then reusing it for conversion of styrene oxide to styrene episulfide at the optimized reaction conditions. The results showed that the regenerated alumina saves its activity for several times (Table 2).

The capability of this synthetic protocol was further investigated with the reaction of activated, deactivated and cyclic epoxides by alumina immobilized thiourea at the optimized reaction condition. Table 3 represents the general trend and versatility of the thiourea/CaCO$_3$ system.

Solvent-free conversion of epoxides to thiiranes with alumina immobilized thiourea, general procedure

A mixture of epoxide (1 mmol) and alumina immobilized thiourea (0.752 g, 25% w/w) was ground in a mortar for 2 min at room temperature to give alumina immobilized thiourea (0.752 g, 25% w/w). FT-IR ($\nu_{\text{max}}$/cm$^{-1}$, KBr): 3383, 3292, 3180, 2366, 2160, 1738, 1513, 1375, 1292, 1198, 1090, 859. FT-IR spectra were recorded on Thermo Nicolet Nexus 670 and Bruker Avance (300 MHz) spectrometers, respectively. The products were characterized by their spectroscopic data and comparison with the reported data in literature.

Preparation of alumina immobilized thiourea

A mixture of thiourea (0.152 g, 2 mmol) and neutral alumina (0.6 g) was placed in a mortar and then well ground for 2 min at room temperature to give alumina immobilized thiourea (0.752 g, 25% w/w). FT-IR ($\nu_{\text{max}}$/cm$^{-1}$, KBr): 3383, 3292, 3180, 2366, 2160, 1738, 1513, 1375, 1292, 1198, 1090, 859. FT-IR spectrum of thiourea, Al$_2$O$_3$, and the thiourea/Al$_2$O$_3$ system are provided as supporting information.

Reusability of recovered Al$_2$O$_3$ in the conversion of styrene oxide to styrene episulfide by use of alumina immobilized thiourea

A mixture of epoxide (1 mmol) and alumina immobilized thiourea (0.752 g, 25% w/w) was ground in a mortar for 2–9 min at room temperature without a solvent. The progress of the reaction was monitored by TLC using n-hexane:EtOAc (5:2) as an
Table 3. Conversion of epoxides to thiiranes by use of alumina immobilized thiourea under solvent-free condition.\textsuperscript{a}

| Entry | Epoxide | Thirane | Time (min) | Yield (%)\textsuperscript{b} | Ref. |
|-------|---------|---------|------------|---------------------|------|
| 1     | Ph\textsuperscript{\textcircled{O}} | Ph\textsuperscript{\textcircled{S}} | 3           | 97                  | 32   |
| 2     | Cl\textsuperscript{\textcircled{O}} | Cl\textsuperscript{\textcircled{S}} | 5           | 94                  | 31   |
| 3     | MeO\textsuperscript{\textcircled{O}} | MeO\textsuperscript{\textcircled{S}} | 2           | 95                  | 31   |
| 4     |  |  | 6           | 96                  | 32   |
| 5     |  |  | 8           | 93                  | 25   |
| 6     |  |  | 5           | 95                  | 25   |
| 7     |  |  | 4           | 95                  | 25   |
| 8     |  |  | 2           | 98                  | 32   |
| 9     |  |  | 4           | 97                  | 32   |
| 10    |  |  | 2           | 95                  | 25   |
| 11    |  |  | 2           | 83                  | 25   |
| 12    |  |  | 3           | 94                  | 32   |
| 13    |  |  | 3           | 94                  | 25   |
| 14    |  |  | 2           | 90                  | 32   |
| 15    |  |  | 2           | 85                  | 31   |
| 16    |  |  | 9           | 91                  | 32   |

\textsuperscript{a}All reactions were carried out with 1 mmol of epoxide in the presence of thiourea (2 mmol) immobilized on Al\textsubscript{2}O\textsubscript{3} (0.6 g) at room temperature and under solvent-free condition.\textsuperscript{b}Yields refer to isolated pure products.
| Epoxide | Thiourea/Al₂O₃ | Thiourea/Al₂O₃ | Thiourea/CaCO₃ | Thiourea/CaCO₃ | Thiourea/Dowex-50WX | Thiourea/Dowex-50WX | Thiourea/NH₄Cl | Thiourea/SiO₂ | Thiourea/120 °C |
|---------|----------------|----------------|---------------|---------------|----------------------|----------------------|---------------|---------------|----------------|
| Ph      | 2 0.6 3 97     | 2 0.6 3 97     | 2 2 1 96      | 2 2 1 96      | 2 0.5 60 93         | 2 0.5 60 93         | 2 0.5 30 95   | 2 2.8 80 95   | 2 15 65        |
| O      | 2 0.6 2 98     | 2 0.6 2 98     | 2 2 5 97      | 2 2 5 97      | 2 0.5 20 95         | 2 0.5 20 95         | 2 0.5 30 96   | 2 2.8 45 93   | 2 60 80        |
| O      | 2 0.6 4 97     | 2 0.6 4 97     | 2 2 1 98      | 2 2 1 98      | 2 0.5 30 96         | 2 0.5 30 96         | 2 0.5 15 93   | 2 2.8 40 92   | 2 60 77        |
| PhO    | 2 0.6 6 96     | 2 0.6 6 96     | 2 2 10 95     | 2 2 10 95     | 2 0.5 20 91         | 2 0.5 20 91         | 2 0.5 73 94   | 2 2.8 12 95   | 2 15 84        |
| O      | 2 0.6 2 90     | 2 0.6 2 90     | 2 2 3 90      | 2 2 3 90      | 2 0.5 60 85         | 2 0.5 60 85         | 2 0.5 40 65   | 2 2.8 190 92  | 2 25 92        |

*aThe present method.*
eluent. After completion of the reaction, the mixture was washed with EtOAc (3 × 5 mL). The combined washing solvents were evaporated under reduced pressure to give the crude thiirane for further purification by a short-column chromatography over silica gel (83–98% yield) (Table 3).

**Recovery of alumina**

After extraction of the crude thiirane, distilled water (15 mL) was added to the reaction vessel followed by stirring for 5 min at room temperature. The alumina was filtered and then dried in an oven for 2 h at 100 °C. The recycled alumina can be reused for immobilization of thiourea.

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**References**

1. Iranpoor, N.; Firouzabadi, H.; Chitsazi, M.; Jafari, A. A. Tetrahedron 2002, 58, 7037-7042.
2. Dittmer, D. C. In: A. R. Katritzky, C. W. Rees (Eds.), Comprehensive Heterocyclic Chemistry; Pergamon: New York, 1984, 7, p. 132.
3. Vedejs, E.; Krafft, G. A. Tetrahedron 1982, 38, 2857-2881.
4. Kiasat, A. R.; Kazemi, F.; Fallah-Mehrjardi, M. Phosphorus Sulfur Silicon Relat. Elem. 2004, 179, 1841-1844.
5. Takido, T.; Kobayashi, Y.; Itabashi, K. Synthesis 1986, 779-780.
6. (a) Bouda, H.; Borredon, M. E.; Delmas, M.; Gaset, A. Synth. Commun. 1987, 17, 943-951; (b) Jankowski, K.; Harvey, R. Synthesis 1972, 627-628; (c) Sander, M. Chem. Rev. 1966, 66, 297-339.
7. Tamami, B.; Kiasat, A. R. Synth. Commun. 1996, 26, 3953-3958.
8. Brimeyer, M. O.; Mehrota, A.; Quici, S.; Nigam, A.; Regen, S. L. J. Org. Chem. 1980, 45, 4254-4255.
9. Iranpoor, N.; Firouzabadi, H.; Jafari, A. A. Phosphorus, Sulfur, Silicon Relat. Elem. 2005, 180, 1809-1814.
10. Eisavi, R.; Zeynizadeh, B.; Baradarani, M. M. Phosphorus Sulfur Silicon Relat. Elem. 2011, 116, 1902-1909.
11. Zeynizadeh, B.; Baradarani, M. M.; Eisavi, R. Phosphorus Sulfur Silicon Relat. Elem. 2011, 116, 2208-2215.
12. Yadav, J. S.; Subba Reddy, B. V.; Baishya, G. Synlett 2003, 396-398.
13. Yadollahi, B.; Tangestaninejad, S.; Habibi, M. H. Synth. Commun. 2004, 34, 2823-2827.
14. Mohammadpoor-Baltork, I.; Khosropour, A. R. Molecules 2001, 6, 996-1000.
15. Salehi, P.; Khodaei, M. M.; Zolfigol, M. A.; Keyvan, A. Synth. Commun. 2003, 33, 3041-3048.
16. Firouzabadi, H.; Iranpoor, N.; Khoshnood, A. J. Mol. Catal. A: Chem. 2007, 274, 109-115.
17. Reddy, C. S.; Nagavani, S. Heteroatom Chem. 2008, 19, 97-99.
18. Bandgar, B. P.; Patil, A. V.; Kamble, V. T.; Totre, J. V. J. Mol. Catal. A: Chem. 2007, 273, 114-117.
19. Yadav, J. S.; Subba Reddy, B. V.; Sengupta, S.; Gupta, M. K.; Baishya, G.; Harshavardhana, S. J.; Dash, U. Monatsh. Chem. 2008, 139, 1363-1367.
20. Kazemi, F.; Kiasat, A. R. Phosphorus Sulfur Silicon Relat. Elem. 2003, 178, 1333-1337.
21. Mohammadpoor-Baltork, I.; Aliyan, H. J. Chem. Res. 2000, 122-123.
22. Kazemi, F.; Kiasat, A. R.; Ebrahimi, S. Synth. Commun. 2003, 33, 595-600.
23. Bandgar, B. P.; Joshi, N. S.; Kamble, V. T. Tetrahedron Lett. 2006, 47, 4775-4777.
24. Mirkhani, V.; Tangestaninejad, S.; Alipanah, L. Synth. Commun. 2002, 32, 621-626.
25. Yadav, J. S.; Subba Reddy, B. V.; Reddy, C. S.; Rajasekhar, K. J. Org. Chem. 2003, 68, 2525-2527.
26. Surendra, K.; Krishnaveni, N. S.; Rama Rao, K. Tetrahedron Lett. 2004, 45, 6523-6526.
27. Tamami, B.; Borujeny, K. P.; Synth. Commun. 2004, 34, 65-70.
28. Tamami, B.; Kolahdoozan, M. Tetrahedron Lett. 2004, 45, 1535-1537.
29. Moghadam, M.; Tangestaninejad, S.; Mirkhan, V.; Shaibani, V. Tetrahedron 2004, 60, 6105-6111.
30. Moghadam, M.; Tangestaninejad, S.; Mirkhan, V.; Mohammadpoor-Baltork, I.; Taghavi, S. A. Catal. Commun. 2007, 8, 2087-2095.
31. Wu, L.; Wang, Y.; Yan, F.; Yang, C. Bull. Korean Chem. Soc. 2010, 31, 1419-1420.
32. Zeynizadeh, B.; Yeghaneh, S. Phosphorus Sulfur Silicon Relat. Elem. 2008, 183, 2280-2286.
33. Zeynizadeh, B.; Yeghaneh, S. Phosphorus Sulfur Silicon Relat. Elem. 2009, 184, 362-368.
34. Kaboudin, B.; Norouzi, H. Synthesis 2004, 2035-2039.
35. Akhlaghinia, B.; Rahimizadeh, M.; Eshghi, H.; Zhaleh, S.; Rezazadeh, S. J. Sulfur Chem. 2012, 33, 351-361.
36. Mirza-Aghayan, M.; Molaei Tavana, M. J. Sulfur Chem. 2015, 36, 30-35.
37. (a) Danks, T. N.; Desai, B. Green Chem. 2002, 4, 179-180; (b) Kaboudin, B.; Nazari, R. Tetrahedron Lett. 2001, 42, 8211-8213; (c) Kaboudin, B. Chem. Lett. 2001, 880-881.
38. (a) Kiasat, A. R.; Kazemi, F.; Fallah-Mehrjardi, M. J. Chin. Chem. Soc. 2007, 54, 1337-1339; (b) Kiasat, A. R.; Kazemi, F.; Fallah-Mehrjardi, M. Asian J. Chem. 2005, 17, 2830-2832; (c) Schmurch, M.; Holzweber, M.; Mihovilovic, M. D.; Stanetty, P. A Green Chem. 2007, 9, 139-145.
39. Lazlo, P. Preparative Chemistry Using Supported Reagents, Academic Press: San Diego, CA, 1987, p. 387.

**Scheme 2.** A proposed mechanism for conversion of epoxides to thiiranes by use of alumina immobilized thiourea.