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Recyclable superparamagnetic Fe_3O_4 nanoparticles for efficient catalysis of thiolysis of epoxides

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ABSTRACT

An efficient and rapid procedure is developed for room-temperature ring opening of various epoxides with thiols under solvent-free conditions in the presence of catalytic amount of superparamagnetic Fe_3O_4 nanoparticles. As a result, high conversion of reactants to various β-hydroxy sulfides is observed in short time periods while the heterogeneous catalyst could be recovered and reused over several cycles without loosing its activity. Competitive reactions show higher reactivity of aromatic thiols over the aliphatic counterparts.

1. Introduction

Nucleophilic ring opening of epoxides with thiols is a very frequently used reaction in synthetic organic chemistry and has found many applications in total synthesis of pharmaceutical [1–3] and natural [4,5] products, especially in the preparation of leukotrienes [6]. The reaction leads to the synthesis of β-hydroxy sulfides for which many synthetic procedures involving thiolysis of epoxides is reported using various methods such as Lewis acid mediation [7–9], aqueous conditions [10–13], heterogeneous catalysis [14,15], and non-conventional bases [16,17]. However, in many of the available methods, the process is performed in a solvent and in the presence of stoichiometric amounts of a Lewis acid or an additive.

Lewis acid catalysis is of fundamental importance in modern synthetic organic chemistry due to allowing efficient interconversion of various functional groups [18]. However, complete decomposition of the catalysts and production of environmentally harmful inorganic salts at workup stage are the drawbacks associated with the use of conventional homogeneous Lewis acids. In contrast, heterogeneous catalysts have been employed extensively in recent years to boost many synthetic transformations in organic chemistry [19,20], since they avoid such limitations, require easier experimental procedures, and involve milder reaction conditions. In addition, minimal waste disposal and reusability of catalysts make heterogeneous systems more attractive from environmental point of view [21,22]. In this context, heterogeneous catalysis using magnetic particles has witnessed a rapid growth in recent years, due to finding numerous applications in nanocatalysis [23–25], biotechnology [26], and medicine [27]. Moreover, the magnetic property of such particles facilitates quantitative recycling of the catalyst by applying an external magnetic field [28].

Recently, we presented an efficient protocol for rapid room-temperature protection of alcohols and phenols with HMDS using superparamagnetic Fe_3O_4 particles [29]. We then reported the application of the method in the multi-component Strecker reaction [30]. In these procedures, after completion of the reactions, the catalyst could be recovered several times using an external magnet and efficiently reused in next reactions, while use of no other additive or co-catalyst was required. In the framework of our studies on the development of green synthetic procedures [31,32] and in continuation of our previous experiences on ring opening reactions of epoxides [33,34], we would like here to report an efficient and novel method for thiolysis of various epoxide rings using catalytic quantities of a magnetically recoverable nanocatalyst while no other additive or solvent is employed (Scheme 1).

2. Experimental

2.1. General

All reported yields are based on isolated compounds. Melting points were determined with a Buchi melting point apparatus and are uncorrected. TLC separations were carried out on silica gel

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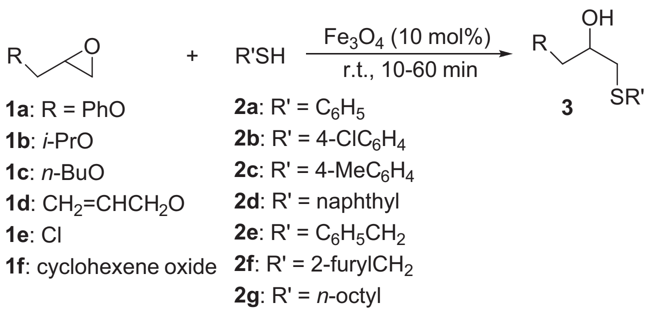

Scheme 1.

Table 1
Fe_3O_4 catalyzed thiolysis of epoxides **1**.

Entry	Epoxide	Thiol	Product	Time (min)	Yield%[a]
1	**1a**	**2a**	**3aa**	10	98
2	**1a**	**2b**	**3ab**	10	93
3	**1a**	**2c**	**3ac**	20	94
4	**1a**	**2d**	**3ad**	20	96
5	**1b**	**2a**	**3ba**	15	89
6	**1b**	**2b**	**3bb**	15	90
7	**1b**	**2c**	**3bc**	20	75
8	**1b**	**2d**	**3bd**	20	79
9	**1c**	**2a**	**3ca**	20	86
10	**1c**	**2b**	**3cb**	20	90
11	**1c**	**2c**	**3cc**	20	65
12	**1d**	**2a**	**3da**	15	88
13	**1d**	**2b**	**3db**	15	87
14	**1d**	**2c**	**3dc**	20	65
15	**1e**	**2a**	**3ea**	15	89
16	**1e**	**2b**	**3eb**	20	85
17	**1f**	**2a**	**3fa**	15	93
18	**1f**	**2b**	**3fb**	20	94
19	**1f**	**2c**	**3fc**	20	81
20	**1a**	**2e**	**3ae**	60	25
21	**1a**	**2f**	**3af**	60	20
22	**1a**	**2g**	**3ag**	60	<5

[a] Isolated yields.

$$\mathbf{1a} + \mathbf{2a} + \mathbf{2e} \xrightarrow[\text{r.t., 10 min}]{Fe_3O_4\text{ (10 mol\%)}} \mathbf{3aa}\ (98\%) + \mathbf{3ae}\ (<5\%)\ [>19:1]$$

$$\mathbf{1a} + \mathbf{2a} + \mathbf{2f} \xrightarrow[\text{r.t., 10 min}]{Fe_3O_4\text{ (10 mol\%)}} \mathbf{3aa}\ (98\%) + \mathbf{3af}\ (<5\%)\ [>19:1]$$

$$\mathbf{1a} + \mathbf{2a} + \mathbf{2g} \xrightarrow[\text{r.t., 10 min}]{Fe_3O_4\text{ (10 mol\%)}} \mathbf{3aa}\ (98\%) + \mathbf{3ag}\ (<5\%)\ [>19:1]$$

Fig. 1. Competitive thiolysis of epoxides.

plates with UV indicator; visualization was by UV fluorescence or by staining with iodine vapor. IR spectra were recorded on a FT-IR Bruker Vector 22 infrared spectrophotometer using KBr disks. NMR spectra were recorded on FT-NMR Bruker Ultra Shield^{TM} (500 MHz) or Bruker AC 80 MHz as $CDCl_3$ solutions with TMS as internal reference. GC–MS were obtained on a Fisons 8000 Trio instrument at an ionization potential of 70 eV. XRD analyses were carried out using a Bruker D_8-advance over the 2θ range from 10° to 70°, using Cu radiation ($\lambda = 1.54060$ Å). Scanning election microphotographs (SEM) were obtained on a Hitachi S-4160.

2.2. Materials

The Fe_3O_4 nanoparticles were prepared according to the known procedure reported by Stroeve and co-workers [35] using $FeCl_2$ and $FeCl_3$ and analyzed using X-ray powder diffraction and scanning election microscopy experiments. Epoxides **1a–f**, thiols **2a–g**, $FeCl_2$, and $FeCl_3$ were purchased from Merck company and were used as received. TLC and column chromatography experiments were carried out using silica gel 60 (Merck, less than 0.063 mm) and ethyl acetate/hexane mixtures (1:4) as the eluent. Solvents were purchased from Merck company.

2.3. Typical procedure

A mixture of 3.0 mmol epoxide, 3.0 mmol thiophenol and Fe_3O_4 (10 mol%) was stirred at room temperature for appropriate length of time until TLC showed completion of the reaction. The mixture was diluted with diethyl ether. A conventional permanent magnet was applied externally on to the outside of the reaction vessel to separate the solid catalyst from the solution. The ethereal phase was washed with saturated solution of $NaHCO_3$ and filtered through a short Na_2SO_4 column. The solvent was removed under reduced pressure and the product was purified using bulb-to-bulb distillation or column chromatography over silica gel, if necessary. The ^{1}H NMR, IR, and GC–MS spectra of the products were obtained and compared perfectly to those existing in the literature. The recycled catalyst was rinsed with ether, dried in oven (50 °C for 2 h), and reused in next reactions.

3. Results and discussion

We first subjected 2-(phenoxymethyl)oxirane **1a** to react with thiophenol **2a** in the presence of Fe_3O_4 to find the optimized conditions. Experiment showed that catalytic quantities of the catalyst (10 mol%) are enough for complete disappearance of the starting materials in 10 min. Use of lower amounts of Fe_3O_4 only prolonged the reaction time or lowered the yield of the reaction. Analysis of the ^{1}H NMR spectrum of the crude mixture showed the formation of β-hydroxy sulfide **3aa** as the sole product of the reaction (Table 1, entry 1). This indicates that the nucleophilic attack of the thiol occurs exclusively at the less hindered side of the epoxide. Under similar conditions, the same epoxide reacted with other aromatic thiols, including electron withdrawing- and electron releasing substituted derivatives (entries 2–4) to give more than 85% yields of **3ab–3ad** within 10–20 min time periods.

To evaluate the selectivity of the present procedure, we decided at this point to conduct competitive reactions in order to find out the relative reactivity of thiols for ring opening of epoxides under the optimized conditions. The results depicted in Fig. 1 show that treatment of epoxide **1a** with an equimolar mixture of thiols **2a** and **2e** in the presence of the catalyst (10 mol%) leads to predominant formation of product **3aa**, while only trace quantities of the other possible product (**3ae**) can be detected leaving **2e** almost intact. Similar results were observed when thiophenol was subjected to react with benzylic type phenols **2f** and **2g**. These observations illustrate that **1a** is much more reactive towards aromatic thiols.

The outcome was next applied to the reactions of **1b** with the same thiols to obtain the respective products **3ba–3bd** in short

Fig. 2. A typical reaction mixture in the absence or presence of a magnetic field.

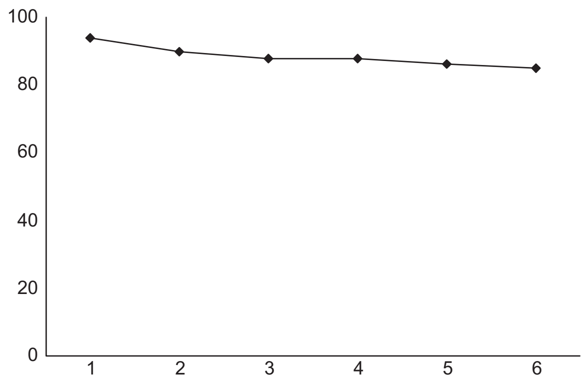

Fig. 3. Efficient recovery of the catalyst.

Table 2
Comparison of the present work with other related procedures for the synthesis of **3fa**.

Conditions	Solvent used	Time	Yield%	Reference
Fe_3O_4	–	15 min	93[a]	–
n-Bu_3P	H_2O	12 h	72[b]	[10]
$Zn(ClO_4)_2{\cdot}6H_2O$	Et_2O	30 min	100[b]	[7]
Borax	H_2O, CH_2Cl_2	2 h	93[a]	[17]
K_2CO_3	Et_2O	12 h	95[a]	[9]
β-Cyclodextrin, 60 °C	H_2O, EtOAc	15 min	80[a]	[11]
NaOH, MW (150 °C)	H_2O, Et_2O	5 min	97[a]	[12]
NaOH (30 °C)	H_2O, Et_2O	3 h	95[a]	[13]
$LiNTf_2$	CH_2Cl_2	20 h	87[a]	[8]

[a] Isolated yield.
[b] GC conversion.

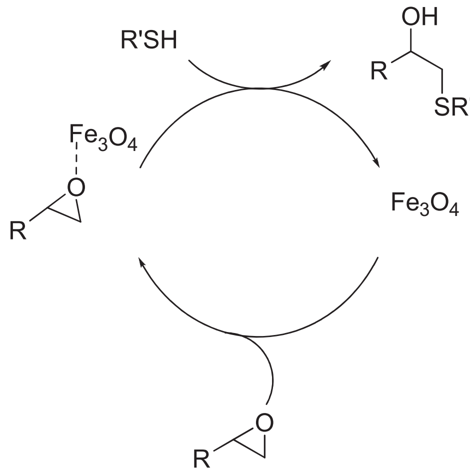

Fig. 5. Proposed mechanism.

time periods (entries 5–8). To further illustrate the applicability of this procedure to other epoxides, we then subjected **1c** and **1d** to the same conditions to evaluate their reactions with thiols **2a–c**. As a result, products **3ca–3cc** (entries 9–11) and **3da–3dc** (entries 12–14) were obtained in high yields within comparable time periods. Epoxide **1e** also behaved equally well in reaction with thiols **2a** (entry 15) and **2b** (entry 16). For ring opening of cyclohexene oxide **1f** with thiols **2a–c**, formation of single products *trans*-2-(arylthio)cyclohexanols **3fa–3fc** was noticed (entries 17–19) within 15–20 min. In all cases, sole formation of single regioisomeric products was observed indicating the high selectivity of the method. At the end of the reactions, mixtures were diluted with Et_2O and the solid catalyst was then separated from the mixtures by applying a magnet on the exterior wall of the reaction tubes. Under the conditions, the same reactions with aliphatic thiols were much less efficient and gave lower quantities of the respective products (entries 20–22).

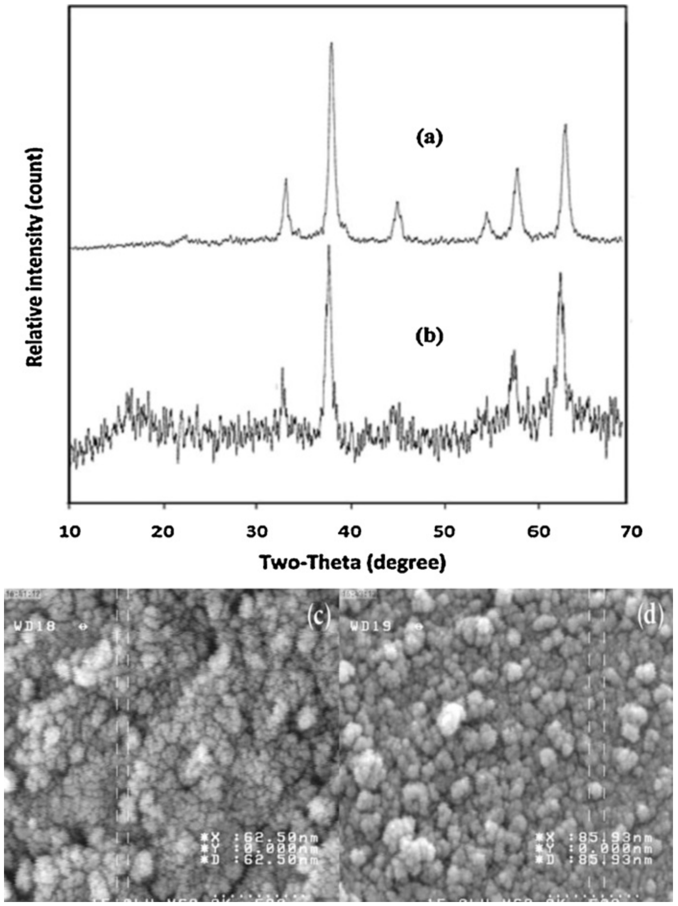

Fig. 4. XRD spectrum of fresh catalyst (a). XRD spectrum of recycled catalyst (b). SEM pattern of fresh catalyst (c). SEM pattern of recycled catalyst (d).

After completion of the reactions, recovery of Fe_3O_4 from the reaction mixtures was easily achieved by applying an external permanent magnet on the outside wall of the reaction tubes, as shown in Fig. 2. Therefore, the products were isolated in good purity after the volatile portions were removed under reduced pressure. Finally, the recovered catalyst was reused successfully in six subsequent reactions without significant loss of activity, as illustrated in Fig. 3.

The structure and the identity of the recovered catalyst were compared with those of fresh Fe_3O_4 by their XRD patterns. The results clearly show that the fresh catalyst (Fig. 4a) still maintains its structure after several recycles (Fig. 4b). In addition, the SEM micrographs of the catalyst show no much particle size difference before (Fig. 4c) and after (Fig. 4d) recycling.

Based on the above results, a pathway can be offered for the reaction (Fig. 5) where Fe_3O_4 is continuously recovered and reused throughout the course of the process. This hypothesis is supported by successful recovery of the catalyst via a simple filtration and its direct reuse for six times in a row without noticeable loss of activity. This is also verified by the fact that the catalyst maintains its structure after recovery, as seen in Fig. 4.

4. Conclusion

In conclusion, we presented a very efficient methodology for rapid ring opening of epoxides with different thiols at room-temperature. Use of catalytic amounts of magnetic Fe_3O_4 in the presence of no extra additive or solvent, easy recovery of the catalyst, high region- and chemoselectivity of the protocol, and environmental safety of the reactions are among the advantages of the present method. We are currently working on the application of this catalyst in other synthetic organic transformations. We believe that Fe_3O_4 can also find applications in industrial processes where the catalyst can be used over several cycles in a continuous manner while the products are discharged after each cycle and the reactor is charged with reactants each time. We can reach at a better conclusion by comparing the performance of the present method with those of other methodologies available in the literature, as summarized in Table 2 for product **3fa**.

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References

[1] F. Viola, G. Balliano, P. Milla, L. Cattel, F. Rocco, M. Ceruti, Bioorg. Med. Chem. 8 (2000) 223–232.
[2] A. Conchillo, F. Camps, A. Messeguer, J. Org. Chem. 55 (1990) 1728–1735.
[3] I.A. Dotsenko, M. Curtis, N.M. Samoshina, V.V. Samoshin, Tetrahedron 67 (2011) 7470–7478.
[4] S. Hammarström, B. Samuelsson, D.A. Clark, G. Goto, A. Marfat, C. Mioskowski, E.J. Corey, Biochem. Biophys. Res. Commun. 92 (1980) 946–953.
[5] J.R. Luly, N. Yi, J. Soderquist, H. Stein, J. Cohen, T.J. Perun, J.J. Plattner, J. Med. Chem. 30 (1987) 1609–1616.
[6] E.J. Corey, D.A. Clark, A. Marfat, G. Goto, Tetrahedron Lett. 21 (1980) 3143–3146.
[7] Shivani, A.K. Chakraborti, J. Mol. Catal. A: Chem. 263 (2007) 137–142.
[8] J. Cossy, V.R. Bellosta, C. Hamoir, J.-R. Desmurs, Tetrahedron Lett. 43 (2002) 7083–7086.
[9] F. Fringuelli, F. Pizzo, S. Tortoioli, L. Vaccaro, Tetrahedron Lett. 44 (2003) 6785–6787.
[10] R.-H. Fan, X.-L. Hou, J. Org. Chem. 68 (2002) 726–730.
[11] M.S. Reddy, B. Srinivas, R. Sridhar, M. Narender, K.R. Rao, J. Mol. Catal. A: Chem. 255 (2006) 180–183.
[12] V. Pironti, S. Colonna, Green Chem. 7 (2005) 43–45.
[13] F. Fringuelli, F. Pizzo, S. Tortoioli, L. Vaccaro, Green Chem. 5 (2003) 436–440.
[14] V. Polshettiwar, M.P. Kaushik, Catal. Commun. 5 (2004) 515–518.
[15] J. Sun, F. Yuan, M. Yang, Y. Pan, C. Zhu, Tetrahedron Lett. 50 (2009) 548–551.
[16] W. Guo, J. Chen, D. Wu, J. Ding, F. Chen, H. Wu, Tetrahedron 65 (2009) 5240–5243.
[17] P. Gao, P.-F. Xu, H. Zhai, Tetrahedron Lett. 49 (2008) 6536–6538.
[18] A. Corma, H. Garcia, Chem. Rev. 103 (2003) 4307–4365.
[19] J.E. Mondloch, E. Bayram, R.G. Finke, J. Mol. Catal. A: Chem. 355 (2012) 1–38.
[20] L. Ronchin, A. Vavasori, L. Toniolo, J. Mol. Catal. A: Chem. 355 (2012) 134–141.
[21] V. Polshettiwar, R.S. Varma, Green Chem. 12 (2010) 743–754.
[22] S.M. Coman, G. Pop, C. Stere, V.I. Parvulescu, J. El Haskouri, D. Beltrán, P. Amorós, J. Catal. 251 (2007) 388–399.
[23] A.-H. Lu, E.L. Salabas, F. Schüth, Angew. Chem. Int. Ed. 46 (2007) 1222–1244.
[24] C.W. Lim, I.S. Lee, Nano Today 5 (2010) 412–434.
[25] V. Polshettiwar, R. Luque, A. Fihri, H. Zhu, M. Bouhrara, J.-M. Basset, Chem. Rev. 111 (2011) 3036–3075.
[26] A.K. Gupta, M. Gupta, Biomaterials 26 (2005) 3995–4021.
[27] M. Mahmoudi, H. Hosseinkhani, M. Hosseinkhani, S. Boutry, A. Simchi, W.S. Journeay, K. Subramani, S. Laurent, Chem. Rev. 111 (2011) 253–280.
[28] M. Kawamura, K. Sato, Chem. Commun. (2006) 4718–4719.
[29] M.M. Mojtahedi, M.S. Abaee, M. Eghtedari, Appl. Organomet. Chem. 22 (2008) 529–532.
[30] M.M. Mojtahedi, M.S. Abaee, T. Alishiri, Tetrahedron Lett. 50 (2009) 2322–2325.
[31] M.S. Abaee, M.M. Mojtahedi, S. Forghani, N.M. Ghandchi, M. Forouzani, R. Sharifi, B. Chaharnazm, J. Braz. Chem. Soc. 20 (2009) 1895–1900.
[32] M.M. Mojtahedi, M. Javadpour, M.S. Abaee, Ultrason. Sonochem. 15 (2008) 828–832.
[33] M.S. Abaee, M.M. Mojtahedi, H. Abbasi, E.R. Fatemi, Synth. Commun. 38 (2008) 282–289.
[34] M.S. Abaee, V. Hamidi, M.M. Mojtahedi, Ultrason. Sonochem. 15 (2008) 823–827.
[35] Y.S. Kang, S. Risbud, J.F. Rabolt, P. Stroeve, Chem. Mater. 8 (1996) 2209–2211.