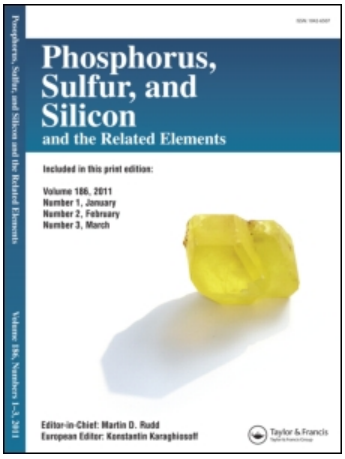


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Facile Room-Temperature $MgBr_2 \cdot OEt_2$-Catalyzed Thiolysis of Epoxides Under Solvent-Free Conditions

Mohammad M. Mojtahedi[a]; M. Saeed Abaee[a]; Mohammad Bolourtchian[a]; Hassan Abbasi[a]
[a] Organosilicon Laboratory, Chemistry and Chemical Engineering Research Center of Iran, Tehran, Iran

To cite this Article Mojtahedi, Mohammad M. , Abaee, M. Saeed , Bolourtchian, Mohammad and Abbasi, Hassan(2007) 'Facile Room-Temperature $MgBr_2 \cdot OEt_2$-Catalyzed Thiolysis of Epoxides Under Solvent-Free Conditions', Phosphorus, Sulfur, and Silicon and the Related Elements, 182: 4, 905 — 910
To link to this Article: DOI: 10.1080/10426500601088697
URL: http://dx.doi.org/10.1080/10426500601088697

Phosphorus, Sulfur, and Silicon, 182:905–910, 2007

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500601088697

Taylor & Francis
Taylor & Francis Group

Facile Room-Temperature $MgBr_2 \cdot OEt_2$-Catalyzed Thiolysis of Epoxides Under Solvent-Free Conditions

Mohammad M. Mojtahedi
M. Saeed Abaee
Mohammad Bolourtchian
Hassan Abbasi
Organosilicon Laboratory, Chemistry and Chemical Engineering Research Center of Iran, Tehran, Iran

Solvent-free ring opening of 1,2-epoxides with aromatic and aliphatic thiols under 1 mol% magnesium bromide ethyl etherate catalysis affords rapid formation of β-hydroxy sulfides at ambient temperature with excellent yields. Nucleophilic attack of the thiols occurs regioselectively at the less hindered position of the epoxides.

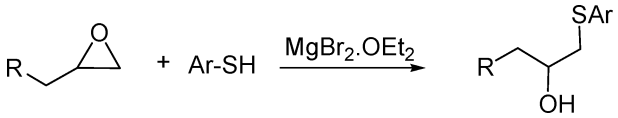
Keywords Epoxides; magnesium bromide catalysis; solvent-free reaction; thiols

Ring opening of epoxides with thiols is an important method in organic synthesis and has found many uses in pharmaceutical[1] and natural product chemistry,[2] particularly for the synthesis of leukotrienes.[3] Recent approaches for the synthesis of β-hydroxy sulfides have been involving a nucleophilic ring opening of epoxides with thiols in the presence of species such as $InCl_3$,[4] $ZnCl_2$,[5] $B(C_6F_5)_3$,[6] ceric ammonium nitrate,[7] hexafluoroisopropanol,[8] lithium bistrifluoromethanesulfonimide,[9] $CoCl_2$,[10] alumina,[11] polyethylene glycol,[12] gallium complexes,[13] $NiCl_2 \cdot 6H_2O$,[14] CsF on celite,[15] lanthanide complexes,[16] tertiary amines,[17] and lithium perchlorate.[18] Microwave-irradiation enhanced methodologies have also been reported very recently.[19] In many of these cases, the ring opening of epoxides is carried out in a solvent and in the presence of equimolar quantities of a Lewis acid or other additives. Recent solvent-free examples conducted under

Received August 14, 2006; accepted September 26, 2006.
Partial financial support by the Ministry of Science, Research, and Technology of Iran is greatly appreciated.
Address correspondence to Mohammad M. Mojtahedi, Chemistry and Chemical Engineering Research Center of Iran, P.O. Box 14335-186, Tehran, Iran. E-mail: mojtahedi@ccerci.ac.ir

Lewis acid catalysis still involves the use of minimum 5 mol% of a relatively expensive catalyst[4b,20] or employs rather complex procedures.[21]

In recent years, magnesium bromide ethyl etherate ($MgBr_2{\cdot}OEt_2$) has found many applications as a mild Lewis-acid to ease various synthetic organic transformations.[22] In this context, we have demonstrated the usefulness of $MgBr_2.OEt_2$ in Diels-Alder cycloadditions,[23] Cannizzaro reactions,[24] aldol condensation,[25] α-aminonitrile syntheses,[26] and alcohols protection.[27] In continuation of these experiences, we would like to introduce now an efficient r.t. procedure for regioselective ring opening of various epoxides with thiols using a very mild and inexpensive medium under solvent-free conditions (Scheme 1).



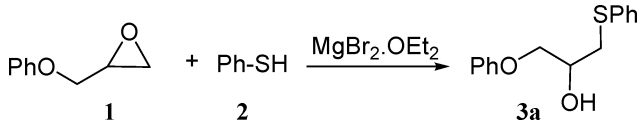
SCHEME 1

Initially, 2-(phenoxymethyl)oxirane **1** was treated with an equimolar amount of thiophenol **2** in the presence of different ratios of $MgBr_2{\cdot}OEt_2$ and under various sets of conditions. Deficient quantities of $MgBr_2.OEt_2$ (1 mol%) proved to be effective for complete conversion of the starting materials to the desired product as shown in Table I. As a result, rapid formation of **3a** was observed in a pattern independent from the type of solvent (Table I, entries 1–8). Faster formation of **3a** was noticed in less than 5 min when no solvent was used in the reaction mixtures (Table I, entries 9–11). Control experiments confirmed the combined promoting and catalytic effects of $MgBr_2{\cdot}OEt_2$; an alternative reaction in the absence of the catalyst led to formation of only 32% of **3a** after 10 h (Table I, entry 12).

The generality of the methodology was demonstrated by subjecting other epoxides to react with various aromatic and aliphatic thiols in the presence 1 mol% of $MgBr_2{\cdot}OEt_2$ and under solvent free conditions (Table II). All experiments were completed in less than 5 min at r.t. as monitored by TLC.

^{1}H NMR spectra of the crude reaction mixtures showed the formation of β-hydroxy sulfides **3a**–**3q** indicating that the nucleophilic attack of the thiols occurred at the less hindered position of the epoxides. In some instances, the presence of the opposite regioisomers was noticed in the crude mixtures in very small amounts ($\sim$1%) proving the high regioselectivity of the reactions. Bulb-to-bulb distillation or column chromatography of the crude mixtures gave more than 90% of the desired products.

TABLE I Optimization of Thiolysis of 1 with 2 under Various Conditions at Ambient Temperature



1 **2** **3a**

Entry	$MgBr_2.OEt_2$ mol%	Solvent	Conversion[a] (%)
1	10.0	THF	95[b]
2	1.0	THF	94[c]
3	10.0	$C_6H_5CH_3$	93[b]
4	1.0	$C_6H_5CH_3$	95[c]
5	10.0	CH_3CN	97[b]
6	1.0	CH_3CN	95[c]
7	10.0	CH_2Cl_2	94[b]
8	1.0	CH_2Cl_2	92[c]
9	10.0	—	95[d]
10	5.0	—	94[d]
11	1.0	—	92[d]
12	—	—	32[e]

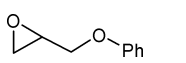
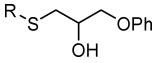
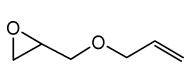
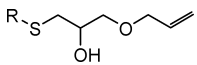
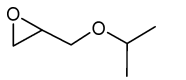
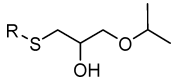
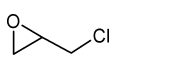
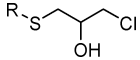
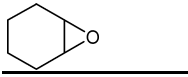
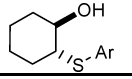
[a]Gas Chromatagrophy yields.
[b]Reactions completed in about 1 h.
[c]Reactions completed in 20–30 min.
[d]Reactions completed within a few minutes.
[e]Reactions completed after 10 h.

In summary, $MgBr_2$·OEt_2-promoted ring opening of epoxides with thiols was carried out in less than 5 min under solvent-free conditions. Reactions proceeded with catalytic amounts of the Lewis acid, and the use of harsh conditions and tedious work-up procedures were avoided. High yields of the products, good regioselectivity of the ring openings, and rapid completion of the reactions are among other advantages of this methodology, which make it an attractive addition to the existing literature.

GENERAL PROCEDURE

A mixture of epoxide (5.0 mmol), thiol (5.2 mmol), and $MgBr_2$·OEt_2 (0.05 mmol) was stirred in a flask. The course of the reaction was monitored by TLC, and complete disappearance of the starting materials was observed within a few minutes. The mixture was dissolved in dichloromethane (10 mL) and washed twice with water (10 mL portions). The organic phase was dried over Na_2SO_4, the solvent was

TABLE II Solvent-Free Thiolysis of Epoxides Under 1 Mol% $MgBr_2.OEt_2$ Catalysis

Epoxide	Thiol	Product		Yield (%)[a]
	4-ClC_6H_4SH 2-naphthylSH cyclohexylSH furan-2-yl-CH_2SH		**3b**: R = 4-ClC_6H_4 **3c**: R = 2 naphthyl **3d**: R = cyclohexyl **3e**: R = CH_2 (furan-2-yl)	95 98 92 95
	C_6H_5SH 4-ClC_6H_4SH 2-naphthylSH		**3f**: R = Ph **3g**: R = 4 ClC_6H_4 **3h**: R = 2-naphthyl	95 97 98
	C_6H_5SH 4-ClC_6H_4SH 2-naphthylSH		**3l**: Ar = Ph **3j**: Ar = 4-ClC_6H_4 **3k**: 2-naphthyl	95 93 96
	C_6H_5SH 4-ClC_6H_4SH 2-naphthylSH		**3l** Ar = Ph **3m**: Ar = 4-ClC_6H_4 **3n**: 2-naphthyl	93 96 91
	C_6H_5SH 4-ClC_6H_4SH 2-naphthyl SH		**3o**: Ar = Ph **3p**: Ar = 4-ClC_6H_4 **3q**: 2-naphthyl	86 84 90

[a]Isolated yields.

removed at reduced pressure, and the product was fractionated by column chromatography over silica gel or purified by bulb-to-bulb distillation, if necessary. The NMR, IR, and GC spectra of the products were obtained and compared with those existing in the literature.

Selected Spectroscopic Data

1-(Naphthalen-2-ylsulfanyl)-3-phenoxypropan-2-ol (3c)

^{1}H NMR: δ 2.70–2.88 (m, 2H), 3.20–3.35 (m, 2H), 3.90–4.01 (m, 2H), 6.75–7.90 (m, 12H). ^{13}C NMR: δ 44.4, 50.0, 68.5, 114.4, 121.5, 125.7, 126.9, 126.5, 127.2, 129.5, 129.0, 135.7, 139.3. MS: *m/z* (%) 310 (41) [M^+], 173 (50), 159 (100), 115 (100), 77 (35). IR (KBr): $\tilde{\nu}$ 3426, 1583, 1071, 738 cm^{-1}. Anal. calcd. for $C_{19}H_{18}O_2S$: C, 73.52; H, 5.84. Found: C, 73.1; H, 5.5.

1-Isopropoxy-3-(phenylsulfanyl)propan-2-ol (3i)

^{1}H NMR: δ 1.13 (d, J = 6.5 Hz, 6H), 2.55–2.70 (m, 1H), 2.93–3.20 (m, 2H), 3.50–3.95 (m, 4H), 7.10–7.45 (m, 5H).^{13}C NMR: δ 22.0, 38.1, 69.5, 71.3, 73.0, 127.5, 128.0, 129.3, 137.5. MS: *m/z* (%) 226 (16) [M^+], 123 (26), 109 (100), 77 (24), 43 (17). IR (KBr): $\tilde{\nu}$ 3431, 1588, 1086, 738 cm^{-1}. Anal. calcd. for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02. Found: C, 63.9; H, 8.3.

1-(4-chlorophenylsulfanyl)-3-isopropoxypropan-2-ol (3j)

^{1}H NMR: δ 1.18 (d, $J = 6.5$ Hz, 6H), 3.02–3.20 (m, 2H), 3.45–3.65 (m, 4H), 3.86–3.92 (m, 1H), 7.26–7.45 (m, 4H). MS: *m/z* (%) 260 (42) [M^+], 157 (97), 143 (100), 99 (63), 73 (57), 43 (76). IR (neat): $\tilde{\nu}$ 3443, 1575, 1093, 747 cm^{-1}. Anal. calcd. for $C_{12}H_{17}ClO_2S$: C, 55.27; H, 6.57. Found: C, 55.2; H, 6.7.

1-Isopropoxy-3-(naphthalen-2-ylsulfanyl)-propan-2-ol (3k)

^{1}H NMR: δ 1.18 (d, $J = 6.5$ Hz, 6H), 3.02–3.20 (m, 2H), 3.45–3.65 (m, 4H), 3.86–3.92 (m, 1H), 7.36–7.85 (m, 7H). ^{13}C NMR: δ 21.7, 37.3, 69.0, 71.5, 73.4, 114.0, 121.9, 125.7, 126.3, 126.5, 127.7, 129.0, 129.6, 135.7, 139.9. MS: *m/z* (%) 276 (13) [M^+], 160 (49), 115 (53), 73 (73), 43 (100). IR (KBr): $\tilde{\nu}$ 3457, 1583, 1040, 738 cm^{-1}. Anal. calcd. for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.4; H, 7.4.

1-Chloro-3-(4-chlorophenylsulfanyl)propan-2-ol (3m)

^{1}H NMR: δ 2.80–2.90 (br s, 1H), 3.10 (dd, $J = 7$, 14.5 Hz, 1H), 3.19 (dd, $J = 5.5$, 14 Hz, 1H), 3.9–3.74 (m, 2H), 3.94–3.98 (m, 1H), 7.26–7.45 (m, 4H).^{13}C NMR: δ 38.1, 48.2, 69.6, 129.0, 130.5, 132.2, 135.4. MS: *m/z* (%) 237 (27) [M^+], 194 (31), 157 (100), 143 (45), 108 (52), 75 (37), 45 (57). IR (neat): $\tilde{\nu}$ 3421, 1572, 1093, 742 cm^{-1}. Anal. calcd. for $C_9H_{10}Cl_2OS$: C, 45.58; H, 4.25. Found: C, 45.7; H, 4.1.

REFERENCES

[1] (a) J. R. Luly, N. Yi, J. Soderquist, H. Stein, J. Cohen, T. J. Perun, et al., *J. Med. Chem.*, **30,** 1609 (1987); (b) D. Amantini, F. Fringuelli, O. Piermatti, and L. Vaccaro, *Arkivoc*, **xi,** 293 (2002).

[2] (a) E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Samuelsson, et al., *J. Am. Chem. Soc.,* **102,** 3663 (1980); (b) E. J. Corey, D. A. Clark, and G. Goto, *Tetrahedron Lett.*, **21,** 3143 (1980).

[3] (a) S. Hammarstrom, B. Samuelsson, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, et al., *Biochem. Biophys. Res. Commum.,* **92,** 946 (1980); (b) E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Samuelsson, et al., *J. Am. Chem. Soc.,* **102,** 1436 (1980).

[4] (a) J. S. Yadav, B. V. S. Reddy, and G. Baishya, *Chem. Lett.*, 906 (2002); (b) F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *Tetrahedron Lett.*, **44,** 6785 (2003); (c) F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *Adv. Synth. Catal.,* **344,** 379 (2002).

[5] (a) D. Amantini, F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *Synlett.*, 2292 (2003); (b) F. Fringuelli, F. Pizzo, S. Tortoioli, and L. Vaccaro, *J. Org. Chem.*, **68,** 8248 (2003).

[6] S. Chandrasekhar, C. R. Reddy, B. N. Babu, and G. Chandrashekar, *Tetrahedron Lett.*, **43,** 3801 (2002).

[7] N. Iranpoor, I. M. Baltork, and F. S. Zardaloo, *Tetrahedron,* **47,** 9861 (1991).

[8] V. Kesavan, D. Bonnet-Delpon, and J. P. Begue, *Tetrahedron Lett.*, **41,** 2895 (2000).

[9] (a) J. Cossy, V. Bellosta, C. Hamior, and J. R. Desmurs, *Tetrahedron Lett.,* **43,** 7083 (2002); (b) J. Cossy, V. Bellosta, V. Alauze, and J. R. Desmurs, *Synthesis*, **15,** 2211 (2002).
[10] J. Iqbal, A. Pandey, A. Shukla, R. R. Srivastava, and S. Tripathi, *Tetrahedron*, **46,** 6423 (1990).
[11] (a) G. H. Posner and D. Z. Rogers, *J. Am. Chem. Soc.*, **99,** 8208 (1977); (b) G. H. Posner and D. Z. Rogers, *J. Am. Chem. Soc.*, **99,** 8214 (1977).
[12] A. K Maiti and P. Bhattacharyya, *Tetrahedron*, **50,** 10483 (1994).
[13] T. Iida, N. Yamamoto, H. Sasai, and M Shibasaki, *J. Am. Chem. Soc.*, **119,** 4783 (1997).
[14] B. K. Sarmah and N. C. Barua, *Tetrahedron,* **47,** 8587 (1991).
[15] V. Polshettiwar and M. P. Kaushik, *Catalysis Commun.* **5,** 515 (2004).
[16] A. E. Vougioukas and H. B. Kagan, *Tetrahedron Lett.,* **28,** 6065 (1987).
[17] J. Wu and H. G. Xia, *Green Chem.,* **7,** 708 (2005).
[18] (a) M. M. Mojtahedi, H. Abbasi, M. S. Abaee, and B. Mohebali, *Monatsh. Chem.*, **137,** 455 (2006); (b) M. Chini, P. Crotti, E. Giovani, F. Macchia, and M. Pineschi, *Synlett*. 303 (1992).
[19] (a) M. M. Mojtahedi, H. Ghasemi, M. S. Abaee, and M. Bolourtchian, *Arkivoc*, 68 (2005); (b) V. Pironti and S. Colonna, *Green Chem.*, **7,** 43 (2005).
[20] F. Fringuelli, F. Pizzo, C. Vittoriani, and L. Vaccaro, *Eur. J. Org. Chem.*, 1231 (2006).
[21] D. Albanese, D. Landini, and M. Penso, *Synthesis*, 34 (1994).
[22] (a) C. Malanga and S. Mannucci, *Tetrahedron Lett.*, **42,** 2023 (2001); (b) S. Yamada, S. Yaguchi, and K. Matsuda, *Tetrahedron lett.*, **43,** 647 (2002); (c) S. K. Tipparaju, S. K. Mandal, S. Sur, V. G. Puranik, and A. Sarkar, *Chem. Commun.*, 1924 (2002); (d) B. Z. Zheng, M. Yamauchi, H. Dei, S. Kusaka, K. Matsui, and O. Yonemitsu, *Tetrahedron Lett.*, **41,** 6441 (2000); (e) A. Vakalopoulos and H. M. Hoffmann, *Org. Lett*., **2,** 1447 (2000); (f) P. Lupattelli, C. Bonini, L. Caruso, and A. Gambacorta, *J. Org. Chem.,* **68,** 3360 (2003); (g) S. K. Tipparaju, V. G. Puranik, and A. Sarkar, *Org. Biomol. Chem*. **1,** 1720 (2003); (h) D. E. Ward, M. J. Hrapchak, and M. Sales, *Org. Lett.*, **2,** 57 (2000).
[23] D. E. Ward and M. S. Abaee, *Org. Lett*., **2,** 3937 (2000).
[24] M. S. Abaee, R. Sharifi, and M. M. Mojtahedi, *Org. Lett.*, **7,** 5893 (2005).
[25] M. S. Abaee, M. M. Mojtahedi, M. M. Zahedi, and R. Sharifi, *Heteroatom Chem.*, **18,** 44 (2007).
[26] M. M. Mojtahedi, M. S. Abaee, and H. Abbasi, *Can. J. Chem.*, 429 (2006).
[27] M. M. Mojtahedi, H. Abbasi, and M. S. Abaee, *J. Mol. Catal. A: Chem.*, **250,** 6 (2006).