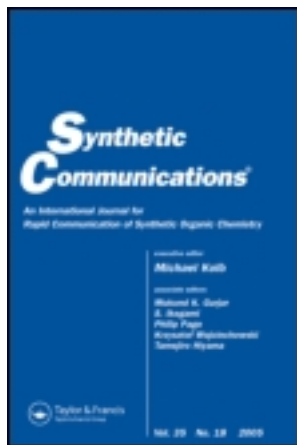


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### Magnesium Hydrogensulfate: A Cheap and Efficient Catalyst for the Conversion of Epoxides into $\beta$ -Alkoxy Alcohols, Vicinal-Diols, and Thiiranes

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## Magnesium Hydrogensulfate: A Cheap and Efficient Catalyst for the Conversion of Epoxides into $\beta$ -Alkoxy Alcohols, Vicinal-Diols, and Thiiranes

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## ABSTRACT

The nucleophilic ring opening reactions of epoxides by aliphatic alcohols and water are achieved efficiently in the presence of catalytic amounts of magnesium hydrogensulfate,  $\text{Mg}(\text{HSO}_4)_2$ , with high degree of regioselectivity. The reactions are chemoselective and many of the other functional groups such as ethereal carbon-oxygen bonds as well as carbon-carbon double bond remain intact under the reaction conditions. Epoxides also react with thiourea or ammonium thiocyanate in the presence of  $\text{Mg}(\text{HSO}_4)_2$  to afford the corresponding thiiranes in good to excellent yields.

*Key Words:* Magnesium hydrogensulfate; Epoxides;  $\beta$ -alkoxy alcohols; Vicinal diols; Thiiranes.

$\beta$ -alkoxy alcohols are commonly synthesized by the alcoholysis of epoxides under acidic conditions.<sup>[1-9]</sup> Hydrolysis of epoxides is an important route to prepare vicinal diols in high yields.<sup>[3,4,8]</sup> Epoxides are also considered as the most convenient starting materials for the synthesis of thiiranes through their reactions with inorganic thiocyanates, thiourea or thioamides in acidic conditions in which oxygen atom is replaced by sulfur.<sup>[10]</sup> When an aqueous solvent is used, control of pH is important to avoid the polymerization of the produced thiiranes.<sup>[11]</sup> Recently, several acidic reagents have been used for this purpose.<sup>[12-17]</sup> But most of these methods suffer from unavailability or high cost of the reagent.

In continuation of our studies on the application of magnesium hydrogensulfate in organic synthesis,<sup>[18]</sup> we wish to report a very efficient and catalytic method for regioselective ring opening of epoxides by alcohols and water.

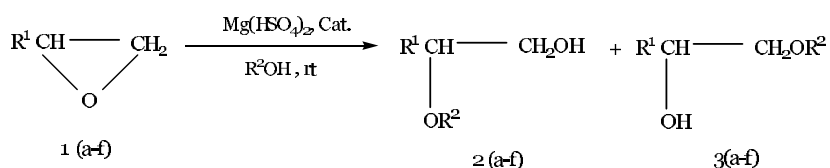
The reaction of epoxides with primary, secondary, and tertiary alcohols in the presence of 0.01–0.2 molar equivalents of  $\text{Mg}(\text{HSO}_4)_2$  was investigated and the corresponding  $\beta$ -alkoxy alcohols were obtained in good to excellent yields with high degree of regio- and chemoselectivity (Sch. 1, Table 1).

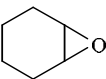
In the case of styrene oxide, the nucleophiles attacked the more hindered carbon (Table 1, Entries 1–5). The alcoholysis reaction of cyclohexene oxide ended up with the formation of trans- $\beta$ -alkoxy alcohols in high yields (Table 1, Entries 6–10). In other model compounds in which electron withdrawing groups were attached to the epoxide ring, the electronic and steric effects act in the same direction and the products of the attack of nucleophiles to the less hindered carbon atoms were obtained (Table 1, Entries 11–29).



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 $\text{R}^2 = \text{Me, n-Pr, i-Pr, t-Bu, Allyl}$ 

R <sup>1</sup> or Epoxide	R <sup>1</sup>
1a Ph-	1d n-BuO-CH <sub>2</sub> -
1b 	1e PhO-CH <sub>2</sub> -
1c CH <sub>2</sub> =CH-CH <sub>2</sub> O-CH <sub>2</sub> -	1f ClCH <sub>2</sub> -

Scheme 1.

The reactions were chemoselective and cleavage of other carbon-oxygen and carbon-halogen bonds was not observed in any case. Also the double bond in allyl glycidyl ether remained intact under the reaction conditions.

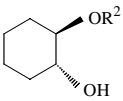
We have also investigated the hydrolysis reactions of epoxides in the presence of catalytic amounts of magnesium hydrogensulfate (Sch. 2, Table 2).

The reactions were carried out in acetone-water (3/1:v/v) as solvent and the corresponding vicinal diols were obtained in excellent yields. In the case of cyclohexene oxide, trans-1,2-dihydroxy cyclohexane was obtained in 95% yield (Table 2, Entry 2).

Different kinds of epoxides were also converted into thiiranes by the reaction with ammonium thiocyanate or thiourea in dry acetonitrile in the presence of 0.5 molar equivalent of magnesium hydrogensulfate (Sch. 3, Table 3).

As shown in Table 3, epoxides bearing electron releasing groups as well as electron withdrawing groups underwent the oxygen-sulfur exchange in high yields. No polymerization product was obtained. The reactions with ammonium thiocyanate took place in 10–30 min while similar reactions with thiourea had taken place in longer periods. This

**Table 1.** The reaction of epoxides with aliphatic alcohols in the presence of magnesium hydrogensulfate at room temperature.

Entry	R <sup>1</sup>	Mg(HSO <sub>4</sub> ) <sub>2</sub> /sub. (mole ratio)	Time (min) [h]	Yield (%)	R <sup>2</sup>	Product
1	1a	0.01	(1)	91	Me	2a
2	1a	0.01	(5)	87	<i>n</i> -Pr	2a
3	1a	0.01	(5)	83	<i>i</i> -Pr	2a(3a trace)
4	1a	0.01	(10)	80	<i>t</i> -Bu	2a(3a trace)
5	1a	0.01	(5)	85	Allyl	2a
6	1b	0.01	(1)	85	Me	
7	1b	0.01	(10)	80	<i>n</i> -Pr	
8	1b	0.01	(10)	83	<i>i</i> -Pr	
9	1b	0.02	(40)	72	<i>t</i> -Bu	
10	1b	0.01	(30)	78	Allyl	
11	1c	0.1	(30)	85	Me	3c
12	1c	0.1	[1]	91	<i>n</i> -Pr	3c
13	1c	0.1	[1.5]	89	<i>i</i> -Pr	3c
14	1c	0.1	[2]	81	<i>t</i> -Bu	3c
15	1c	0.1	[1.3]	85	Allyl	3c
16	1d	0.1	(45)	93	Me	3d
17	1d	0.1	[2]	91	<i>n</i> -Pr	3d
18	1d	0.1	[1.5]	83	<i>i</i> -Pr	3d
19	1d	0.1	[2]	85	<i>t</i> -Bu	3d
20	1d	0.1	[1]	80	Allyl	3d
21	1e	0.1	[1]	95	Me	3e
22	1e	0.1	[3.5]	82	<i>n</i> -Pr	3e
23	1e	0.1	[2.5]	95	<i>i</i> -Pr	3e
24	1e	0.1	[5.5]	85	<i>t</i> -Bu	3e
25	1e	0.1	[1.5]	87	Allyl	3e
26	1f	0.2	[3.5]	82	<i>n</i> -Pr	3f
27	1f	0.2	[4]	80	<i>i</i> -Pr	3f
28	1f	0.2	[8.5]	85	<i>t</i> -Bu	3f
29	1f	0.2	[3]	79	Allyl	3f

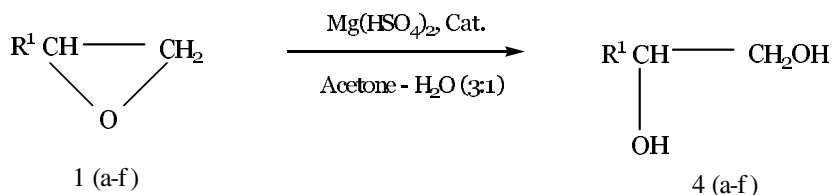
could be due to the higher nucleophilicity of thiocyanate ion in comparison with thiourea.

In conclusion, catalytic nature of the reactions, high degree of regio- and chemoselectivity, cheapness and ease of handling of the reagent are among the outstanding features that make magnesium hydrogensulfate the reagent of choice for the synthesis of  $\beta$ -alkoxy alcohols, vicinal diols and thiiranes from epoxides.



## Magnesium Hydrogensulfate

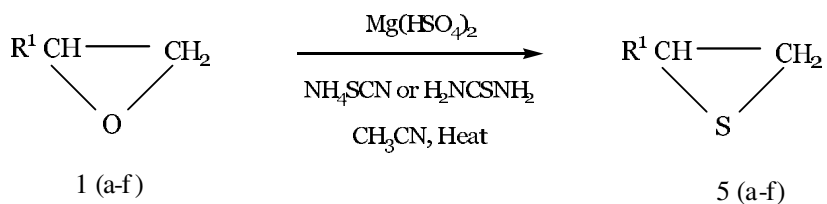
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Scheme 2.

Table 2. Hydrolysis of epoxides in the presence of magnesium hydrogensulfate.

Entry	R <sup>1</sup>	Mg(HSO <sub>4</sub> ) <sub>3</sub> /sub. (mole ratio)	Time (min) [h]	Temp.	Yield (%)	Product
1	1a	0.01	(1)	rt	93	4a
2	1b	0.01	(1)	rt	95	Trans-1,2- cyclohexandiol
3	1c	0.05	[1.5]	reflux	89	4c
4	1d	0.01	(30)	reflux	91	4d
5	1e	0.1	[2]	reflux	93	4e
6	1f	0.1	[1.8]	reflux	90	4f



Scheme 3.

## EXPERIMENTAL

All of the products are known compounds and were characterized by comparison of their spectral data (<sup>1</sup>H NMR, IR) and physical properties with those reported in the literature.<sup>[3,6,13,15]</sup> <sup>1</sup>H NMR spectra were run on a Bruker Avance 500 MHz spectrometer. IR spectra were obtained by a Shimadzu 470 spectrophotometer. The reaction monitoring

**Table 3.** Conversion of epoxides into thiiranes by the reaction with ammonium thiocyanate or thiourea in the presence of magnesium hydrogensulfate.

Entry	R <sup>1</sup>	Nucleophile	Time (min) [h]	Yield (%)	Product
1	1a	NH <sub>4</sub> SCN	(10)	97	5a
2	1b	NH <sub>4</sub> SCN	(20)	95	5b
3	1c	NH <sub>4</sub> SCN	(30)	89	5c
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CH <sub>2</sub>	NH <sub>4</sub> SCN	(20)	92	5[R <sup>1</sup> =CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CH <sub>2</sub> ]
5	1e	NH <sub>4</sub> SCN	(30)	85	5e
6	1f	NH <sub>4</sub> SCN	(25)	90	5f
7	1a	H <sub>2</sub> NCSNH <sub>2</sub>	[2.5]	80	5a
8	1b	H <sub>2</sub> NCSNH <sub>2</sub>	[2]	87	5b
9	1c	H <sub>2</sub> NCSNH <sub>2</sub>	[7]	81	5c
10	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CH <sub>2</sub>	H <sub>2</sub> NCSNH <sub>2</sub>	[5]	90	5[R <sup>1</sup> =CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CH <sub>2</sub> ]
11	1e	H <sub>2</sub> NCSNH <sub>2</sub>	[7]	85	5e
12	1f	H <sub>2</sub> NCSNH <sub>2</sub>	[6]	78	5f

was accomplished by TLC on SIL G/UV 254 sheets or by GC on a Shimadzu 8A gas chromatograph. All yields refer to isolated products.

#### General Procedure for the Alcoholysis of Epoxides

Magnesium hydrogensulfate (0.02–0.4 mmol) was added to a solution of epoxide (2 mmol) in alcohol (7 mL). The mixture was stirred magnetically at room temperature for the appropriate period of time (Table 1). The progress of the reaction was followed by GC or TLC. After completion of the reaction, solvent was evaporated under reduced pressure. Water (20 mL) was added and the mixture extracted with diethyl ether (3 × 20 mL). The organic layer was separated and dried (Na<sub>2</sub>SO<sub>4</sub>). Evaporation of the solvent followed by purification on a short silica gel column gave the desired β-alkoxy alcohols in 73–95% yields.

#### General Procedure for the Hydrolysis of Epoxides

To a solution of epoxide (2 mmol) in acetone–water (3/1:v/v, 7 mL), magnesium hydrogensulfate (0.02–0.2 mmol) was added. The reaction mixture was stirred magnetically at the optimum temperature for the

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appropriate period (Table 2). Solvent was evaporated under reduced pressure. Diethyl ether (50 mL) was added and the mixture passed through a silica gel pad followed by washing the pad with ether. Ethereal solution was dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to afford the corresponding vicinal diols in 82–92% yields.

**General Procedure for the Conversion of Epoxides into Thiiranes**

In a round-bottomed flask equipped with a condenser and a magnetic stirrer, a solution of epoxide (2 mmol) in acetonitrile (7 mL) and ammonium thiocyanate/ or thiourea (6 mmol) was prepared. Magnesium hydrogensulfate (1 mmol) was added and the mixture was stirred magnetically under reflux conditions for the appropriate period (Table 3). Progress of the reaction was monitored by TLC (eluent: *n*-hexane/EtOAc:4/1). Solvent was evaporated on a rotary evaporator. Water (15 mL) was added and the mixture extracted with chloroform ( $3 \times 15$  L). The organic layer was separated and dried ( $\text{MgSO}_4$ ). Evaporation of the solvent followed by chromatography on a short column of silica gel gave the pure thiiranes.

**ACKNOWLEDGMENT**

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