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ORIGINAL PAPER

Simple and highly efficient catalyst- and waste-free ring opening of epoxides with Na_2S in water

Najmedin Azizi · Elham Akbari · Frough Ebrahimi · Mohammad R. Saidi

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Abstract Water was found to be a highly efficient and green catalyst and solvent for ring-opening reaction of epoxides with Na_2S at room temperature to give substituted bis(hydroxyethyl)thioethers in high yields.

Keywords Epoxide · Sodium sulfide · Catalyst-free · Water chemistry · Bis(hydroxyethyl)thioethers

Introduction

Epoxides are very useful intermediates and starting materials in organic synthesis due to their versatility and reactivity with a wide range of nucleophiles [1, 2]. They are important functional groups of natural products [3–5], and medicinal [6], polymer [7, 8], and supramolecular [2, 9] compounds. Thiolysis of 1,2-epoxides by sulfur nucleophiles is a convenient, practical, and widely employed strategy for synthesis of *β*-hydroxy sulfides, which are important intermediates in synthesis of drugs, pharmaceuticals [10–12], and natural products [13]. They are also versatile building blocks for synthesis of cyclic sulfides [14, 15], benzoxathiepines, benzothiazepines, and thioketones [16–18]. Therefore, their syntheses have been extensively investigated with different methods in recent years [19–25].

However, among the reactions of sulfur nucleophiles with epoxides, to the best of our knowledge there are no reports in the literature that allow direct access to thiobis(alcohols) by reaction of epoxides with Na_2S without catalyst in water. Recently hexamethyldisilathiane has been used as sulfur nucleophile for ring opening of epoxides in the presence of tetrabutylammonium fluoride (TBAF) as catalyst to produce bis(hydroxyethyl)thioethers in tetrahydrofuran (THF) [26].

Over the last decade governmental policies have been aimed at limiting use of hazardous solvents released into the environment, and their replacement with water is recommended. In this context, environmentally benign chemical processes in water have attracted more attention due to its being a relatively green and cheap media for organic reactions [27–31].

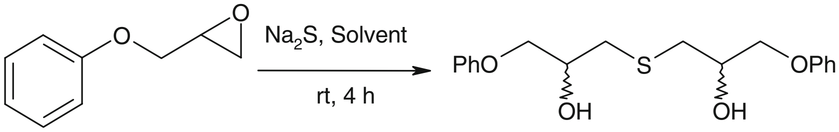
Results and discussion

In continuation of our research interest in developing green organic chemistry by using water as reaction medium [32–35] or by performing organic transformations under solvent-free conditions [36–38], herein we report an efficient, environmentally benign, and simple ring-opening reaction of epoxides with Na_2S under mild conditions. By omitting any organic solvent or catalyst, and reducing the amount of waste, the reaction can be carried out under cleaner reaction conditions at room temperature in water.

N. Azizi (✉)
Chemistry and Chemical Engineering Research Center of Iran,
P.O. 14335-186, Tehran, Iran
e-mail: azizi@ccerci.ac.ir

E. Akbari · F. Ebrahimi · M. R. Saidi (✉)
Department of Chemistry,
Sharif University of Technology,
P.O. Box 11465-9516, 11365 Tehran, Iran
e-mail: saidi@sharif.edu

Scheme 1



Solvent	CH_2Cl_2	$ClCH_2CH_2Cl$	CH_3CN	Ether	Solvent-free	Water
Yield (%)	0	0	35	40	70	97

We wished to explore the applicability of Na_2S, which might act as an acceptable, nontoxic, low cost, and odorless sulfur nucleophile for ring-opening reaction of epoxides, while giving interesting biological compounds. First, we embarked upon a series of experiments to establish the optimum conditions for thiolysis of an epoxide. The reaction between glycidyl phenyl ether and Na_2S was chosen, and the results are presented in Scheme 1. First findings indicated that water was an excellent solvent for thiolysis of glycidyl phenyl ether without using any catalyst or promoter at room temperature to give bis(hydroxyethyl) thioethers with excellent yield. As mentioned above, this reaction yields bis(hydroxyethyl)thioethers, and in order to obtain mono epoxide addition, subsequent reactions with glycidyl phenyl ether were carried out using different amounts of Na_2S. This variation did not change the product distribution, and only in some cases were trace amounts of hydroxyethylthiols observed. We also investigated the effects of common organic solvents, in particular their influence on the rate and course of these reactions. In CH_2Cl_2 or $ClCH_2CH_2Cl$ the reaction did not take place and the starting materials were recovered, and low yield of the product was observed in acetonitrile and diethyl ether (Scheme 1).

Having established optimal conditions for the reaction between glycidyl phenyl ether and Na_2S, we were keen to expand the scope of this reaction and determine whether it would prove equally successful with a range of other epoxides. We therefore examined the reaction of Na_2S with a variety of epoxides under the optimized conditions, and the results are shown in Table 1.

The range of suitable epoxides explored includes commercially available aliphatic epoxides such as glycidyl phenyl ether, propylene oxide, butylene oxide, cyclohexene oxide, and styrene oxide. The results indicate the usefulness of this method. The substituents do not show any significant effects on reaction time or product yields. The regioselectivity in the reaction of unsymmetrical epoxides is governed by both steric and electronic effects. The regioselectivity was determined by ^1H nuclear magnetic resonance (NMR). Unsymmetrical oxiranes underwent cleavage by Na_2S with preferential attack at the less substituted carbon of the epoxide, affording a single product in high to quantitative yields. The only exception was styrene oxide, from which two regioisomers were formed (Scheme 2).

Furthermore, in the case of cyclic epoxides such as cyclohexene oxide (Table 1, entry 12), *trans* products were obtained (Scheme 3). However, there was no significant selectivity for one of the diastereoisomers, and a mixture of two diastereoisomers was obtained (Fig. 1).

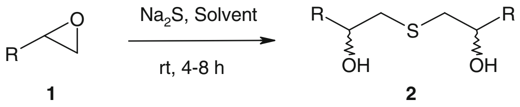
In summary, this simple and easily reproducible coupling of epoxides with Na_2S under catalyst-free conditions in green and abundant solvent affords various bis(hydroxyethyl) thioethers of potentially high synthetic utility in high yield, without the formation of any undesirable side-products.

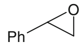
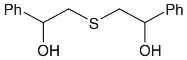
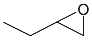
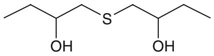
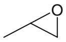
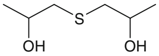
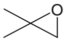
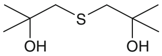
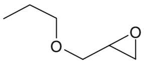
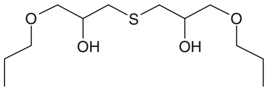
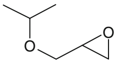
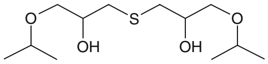
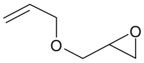
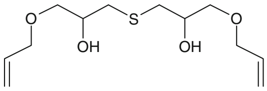
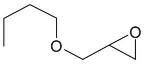
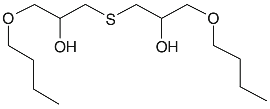
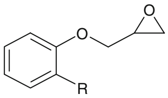
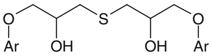
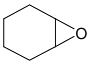
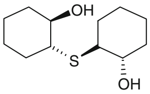
Experimental

General procedure for aqueous ring opening of epoxides with Na_2S

To a stirred solution of 0.4 cm^3 glycidyl phenyl ether (3 mmol) in 2 cm^3 water in a test-tube was added 0.2 g Na_2S (3 mmol), and the resulting mixture was stirred at room temperature for 4–8 h. In the case of solid bis(hydroxyethyl)thioethers, pure products were isolated by filtration. The liquid bis(hydroxyethyl)thioethers were extracted by ethyl acetate and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded the desired pure product in most cases. In a few cases, the crude product was further purified by flash column chromatography to provide the corresponding pure product. All

Table 1 Water-accelerated reaction of epoxides with Na_2S



Entry	Epoxide		Product	Yield[a]	Ref.
1		**2a**		80 (82:18)[b]	[25]
2		**2b**		82	[26]
3		**2c**		78	[25]
4		**2d**		72	[20]
5		**2e**		78	[20]
6		**2f**		95	[25]
7		**2g**		88	[22]
8		**2h**		82	[25]
9		**2i**		97 (R=H)	[25]
10		**2j**		95 (R=Me)	[25]
11		**2k**		92 (R=OMe)	[21, 25]
12		**2l**		70	[25]

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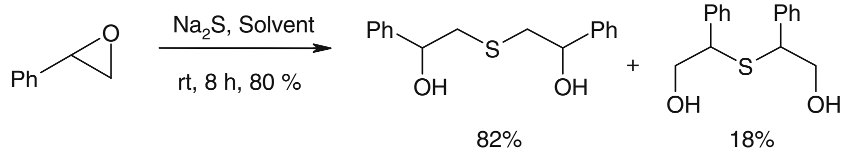
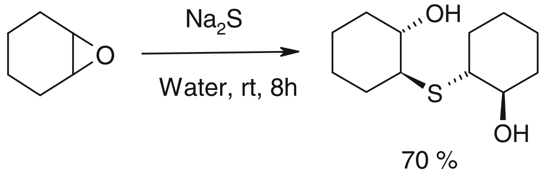
[a] Nuclear magnetic resonance (NMR) yields

[b] See Scheme 2

Scheme 2





Scheme 3

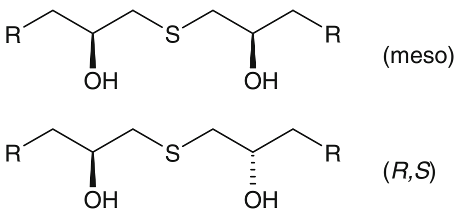


Fig. 1 Possible diastereoisomers

compounds were characterized on the basis of their spectroscopic data (IR and NMR).

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