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Short Report

$Bi(OTf)_3$ or $Bi(TFA)_3$ Catalyzed Efficient, Regio- and Chemoselectively Synthesis of β-Hydroxy Thioethers from Aryl Disulfides in the Presence of Zinc Powder

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Um método novo e conveniente foi desenvolvido para a síntese de β-tioéteres com disulfetos arílicos e zinco em pó, na presença catalítica de $Bi(OTf)_3$ e $Bi(TFA)_3$ em acetonitrila. O presente método é bastante simples e tolera uma variedade de grupos ácidos protetores. Entretanto, disulfetos arílicos e benzílicos não fornecem os correspondentes tioéteres nas mesmas condições. Assim, a regio- e quimiosseletividade observada pode ser apontada como uma vantagem destacada deste método.

A new convenient method has been developed for the synthesis of β-hydroxy thioethers with aryl disulfides and zinc powder in the presence of catalytic amounts of $Bi(OTf)_3$ and $Bi(TFA)_3$ in acetonitrile. The present method is very simple and the conditions tolerate a variety of acid-sensitive protecting groups. On the other hand, alkyl or benzyl disulfides afforded no corresponding thioethers under similar conditions. Then the observed regio- and chemoselectivity can be considered as a noteworthy advantage of this method.

Keywords: β-hydroxy thioethers, epoxides, disulfides, Bi(III) compounds, zinc

Introduction

Ring-opening reaction of epoxides with nucleophiles has been widely used to the preparation of some starting materials that are very important in organic synthesis. Among them thiolyzation of epoxides has attracted much attention because it produces β-hydroxy thioethers as valuable intermediates for the synthesis of important compounds such as α-thioketones,[1] β-hydroxy sulfoxides,[2,3] benzothiazepines[4] or benzoxathiepines[5] that are used as building blocks for preparation of some natural products[6-10] or pharmaceuticals.[11,12] The classical synthesis of β-hydroxy thioethers consists of heating an epoxide with an excess of unpleasant odor thiol. A number of different Lewis acids have been used for this transformation.[13-21] However, some of these methods suffer from one or more limitations including the use of stoichiometric amounts of the reagents and unpleasant odor substrates, long reaction times, unsatisfactory yields, poor selectivity, and the use of expensive and toxic reagents or catalysts. Therefore, to find out a better alternative method for synthesis of β-hydroxy thioethers is desirable.

The applications of bismuth (III) compounds to organic transformations have been extensively studied.[22-26] Many recent papers describing the use of bismuth compounds in organic transformations pointed out that their use is ecologically friendly. In addition, bismuth derivatives have been widely used in medicine.[27] They have attracted much attention because they are easy to handle, low in cost and relatively insensitive to air and moisture.[28]

Very recently, we introduced bismuth (III) salts as efficient catalysts for the ring opening of epoxides with anilines,[29,30] synthesis of β-enaminones,[31] dihydropyrimidones,[32] azalactones[33] and conversion of thiocarbonyls to their carbonyl compounds.[34] In continuation of our interest in exploring new reactions on epoxides catalyzed with bismuth (III) salts, and due to the lack of any report on the ring opening of oxiranes with disulfides in the presence of these Lewis acids, we now report for the first time the thiolysis of oxiranes with aryl disulfides using zinc powder in the presence of 3 mol % of $Bi(TFA)_3$ or 1 mol % $Bi(OTf)_3$ in acetonitrile under reflux conditions (Scheme 1).

Results and Discussion

A variety of epoxides underwent smooth transformation to the corresponding β-hydroxy thioethers in good to excellent yields when they reacted with diaryl disulfides (Table 1). Diphenyl, di-2-naphtyl and di-p-tolyl

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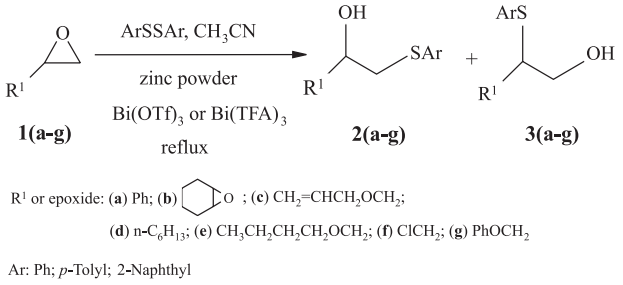


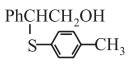
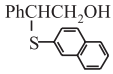
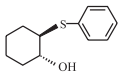
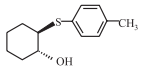
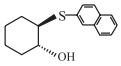
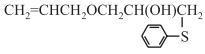
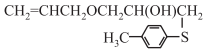
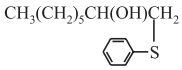
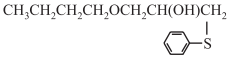
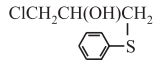
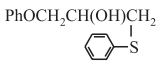
Scheme 1.

disulfides were used as aromatic disulfides in these reactions. Cyclohexene oxide as a symmetrical epoxide underwent cleavage with the aryl disulfides to produce the corresponding β-hydroxy thioethers in high yields and stereo-selectivity (Table 1, entries 4-6). The products obtained from this epoxide showed the formation of *trans* isomer as the only product of the reaction based on ^{1}H NMR spectrum. The reaction of styrene oxide with diaryl disulfide afforded only one product, 2, which was formed from attack of the nucleophile at the benzylic position and its structure was also confirmed by ^{1}H NMR spectroscopy of the crude product (Table 1, entries 1-3). This regio-selectivity is not similar to that obtained from thiolysis of epoxides in tetrabutylammonium fluoride in which the regio-isomer 3 is the major product.[35] This regio-selectivity observed in these reactions seems to be controlled by electronic effects and attack of nucleophile occurs on the carbon atom which can effectively stabilize the developing positive charge. The reaction of alkyl oxirane such as 1,2-epoxyoctane with disulfides underwent in preferential attack at the less crowded side of oxirane and the corresponding β-hydroxy thioether is obtained in high yield and regio-selectivity (Table 1, entry 9).

When the reaction was carried out in the absence of the Lewis acid no product obtained which shows that the presence of the Lewis acid is necessary. The reaction in the presence of catalytic amount of trifluoromethane sulfonic acid as the catalyst in acetonitrile was also examined in order to understand which of the salt (bismuth salt) or the Bronsted acid (trifluoromethane sulfonic acid) has the key role in this reaction. We found that the reaction was proceeded by CF_3SO_3H to afford the corresponding product in less than 1 h. However, since the solvent of the reaction is aprotic in contrast to the solvent (H_2O/THF) used by Mohan's group[36] it seems in this conditions the Lewis acid catalyses the reaction. In other words, under this circumstance the existence of equilibrium between Bi salts and their acids is doubtful. When the same experiments were carried out using $BiCl_3$ and $CeCl_3$, interesting results were obtained. The reaction in the presence of $CeCl_3$ was not performed but, the reaction in the presence of $BiCl_3$ underwent well and gave the same products which shows that the Lewis acid catalyses the reaction. However, since the catalytic amount of trifluoromethane sulfonic acid could also catalyze the reaction under the same reaction conditions, the role of this acid in the reaction can not be eliminated completely. This may be explained by the fact that the used acetonitrile was not completely dried.

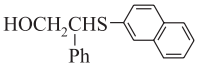
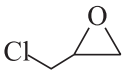
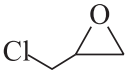
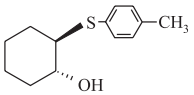
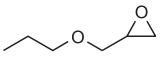
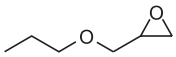
In these reactions 1 mol % of $Bi(OTf)_3$ is sufficient to be effective but in the case of $Bi(TFA)_3$, 3 mol % of the

Table 1. Regioselective ring opening of epoxides with aryl disulfides and zinc powder by $Bi(OTf)_3$ and $Bi(TFA)_3$ in actonitrile

Entry	Aryl	Product[a]	Yield (%)[b]/time (min)	
			$Bi(OTf)_3$	$Bi(TFA)_3$
1 **(1a)**	Ph		92/30	94/30
2 **(1a)**	*p*-Tolyl		90/25	92/25
3 **(1a)**	2-Naphthyl		85/30	86/30
4 **(1b)**	Ph		83/30	83/30
5 **(1b)**	*p*-Tolyl		86/30	88/30
6 **(1b)**	2-Naphthyl		80/30	79/30
7 **(1c)**	Ph		82/45	85/45
8 **(1c)**	*p*-Tolyl		80/45	80/45
9 **(1d)**	Ph		82/30	79/30
10 **(1f)**	Ph		80/70	83/70
11 **(1g)**	Ph		84/50	84/50
12 **(1h)**	Ph		88/45	89/45

[a] All products are known compounds and characterized by comparison of their ^{1}H NMR, ^{13}C NMR, IR spectral data with those reported in literature;[35,18,38] [b] Isolated yields.

Table 2. Competitive reaction of epoxides wih aryl disulfides catalyzed by Bi(III) salts

Epoxide	Aryl disulfide	Product	Yield (%)/ time(min)	
			$Bi(TFA)_3$	B: $Bi(OTf)_3$
	$(2\text{-NaphthylS})_2$		80/35	83/35
			100	100
	$(p\text{-}CH_3C_6H_4S)_2$		83/30	85/30
			100	100

catalyst is required to complete the reactions. In addition the results show that the reactivity of $Bi(OTf)_3$ is more than the reactivity of $Bi(TFA)_3$ in these reactions. We also found that dibenzyl disulfide and dicyclohexyl disulfide as aliphatic disulfides gave no corresponding β-hydroxy thioethers under similar reaction conditions.

To show the potential of the selectivity of these reactions further, the competitive reactions have been carried out and a sample of the results was indicated in Table 2.

Experimental

General

Products were characterized by comparison of their spectroscopic data (^{1}H NMR, IR) with those reported in the literature. All yields refer to isolated products. The products were purified by column chromatography or preparative TLC using SiO_2 as stationary phase.

General procedure forsynthesis of β-hydroxy thioethers

To a mixture of epoxide (1 mmol), aryl disulfide (1 mmol), zinc powder (1 mmol) in acetonitrile (2 mL), $Bi(OTf)_3$ (0.01 mmol) or $Bi(TFA)_3$ (0.03-0.04 mmol) was added and the reaction mixture stirred magnetically under reflux conditions for appropriate time (Table 1). The progress of the reaction was followed by TLC (eluent: n-heptane/ethyl acetate: 3/1). After completion of the reaction, the reaction mixture was filtered and washed with Et_2O (3x10 mL). The organic layer was dried by anhydrous $MgSO_4$ and evaporation of the solvent gave the corresponding crude products, which were purified by column chromatography to afford the pure β-hydroxy thioethers in 79-94% yields (see Table 1). $Bi(OTf)_3$ and $Bi(TFA)_3$ were prepared according to the reported procedures.[37]

Conclusions

It was introduced a convenient and efficient method for the cleavage of epoxides with odorless disulfides regio-and chemo-selectively under relatively mild reaction conditions. The other advantages of this method including catalytic nature, stability and low toxicity of the catalysts, short reaction times and easy work up procedure make it as a useful process for the synthesis of β-hydroxy thioethers.

Supplementary Material

Supplementary data are available free of charge as PDF file at http://jbcs.sbq.org.br.

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