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A facile and efficient method for the rearrangement of aryl-substituted epoxides to aldehydes and ketones using bismuth triflate

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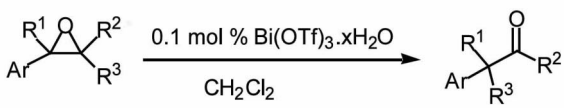
Abstract—Aryl-substituted epoxides undergo smooth rearrangement in the presence of 0.01–0.1 mol% $Bi(OTf)_3 \cdot xH_2O$. The rearrangement is regioselective with aryl-substituted epoxides, and products arise from cleavage of the benzylic C—O bond. The highly catalytic nature of this method coupled with the fact that the reagent is relatively non-toxic, easy to handle and inexpensive make it an attractive alternative to more corrosive and toxic Lewis acids, such as $BF_3 \cdot Et_2O$, currently used to effect epoxide rearrangements.

Keywords: bismuth and compounds, epoxides, rearrangements.

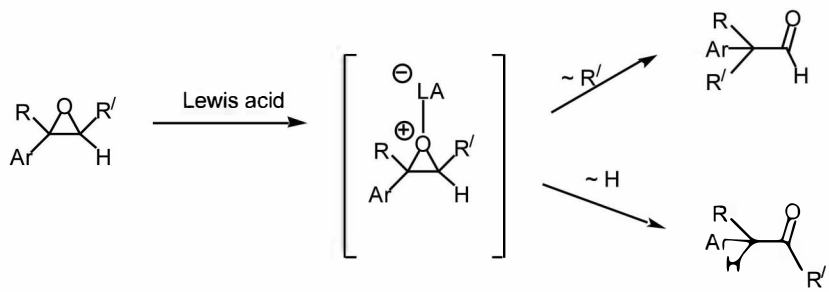
The rearrangement of epoxides to carbonyl compounds is a useful synthetic transformation and hence several reagents have been utilized for this purpose.[1,2] The constitution of the rearrangement product is determined by the identity of the Lewis acid, the migratory aptitude of the epoxide substituents, and the solvent (Scheme 1).

Despite the number of methods that have been developed for epoxide rearrangement, only a few are both regioselective and catalytic in nature. With increasing environmental concerns, it is imperative that new 'environment friendly' reagents be developed.[3] Recently, bismuth compounds have become attractive candidates for use as reagents in organic synthesis due to their low toxicity.[4,5] In an earlier study, we discovered that bismuth(III) oxide perchlorate, $BiOClO_4 \cdot xH_2O$ (20 mol%) is an efficient reagent for the rearrangement of epoxides to carbonyl compounds.[6] A continued search for a more efficient bismuth-based catalyst for epoxide rearrangement formed the basis of this study. We now wish to report that bismuth triflate is a highly efficient catalyst for rearrangement of aromatic epoxides to carbonyl compounds (Eq. (1)). Bismuth triflate has been used as a catalyst for Friedel–Crafts acylations,[7] sulfonylation of arenes,[8] Diels–Alder reactions[9] and aza-Diels–Alder reactions.[10]



(1)

The results of this study are summarized in Table 1. Bismuth triflate is not commercially available but can



Scheme 1.

Table 1. Rearrangement of epoxides with $Bi(OTf)_3 \cdot x H_2O$ in CH_2Cl_2

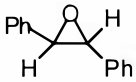
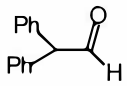
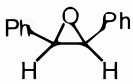
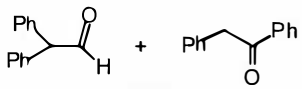
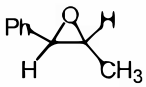
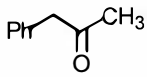
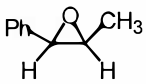
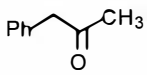
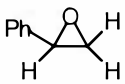
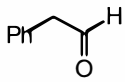
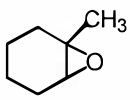
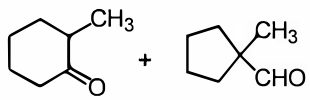
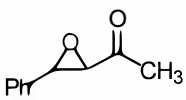
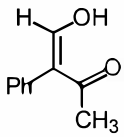
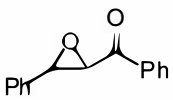
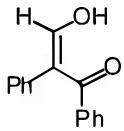
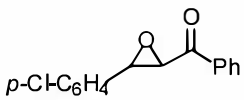
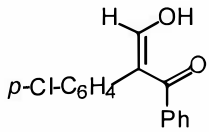
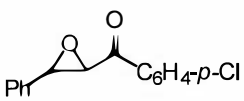
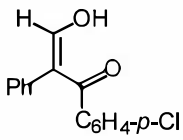
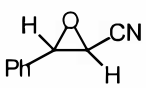
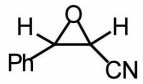
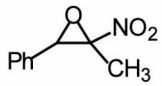
Entry[a]	Epoxide	Time[b]	Product	Yield (%)
1		20 min		92[c]
2		30 min	 (91:9)[e]	89[c]
3		1 h		77[d]
4		1 h		75[d]
5		5 min		73[d]
6		5 min	 (89:11)[e]	74[d]
7[14]		20 min		89[c]
8[15]		20 min		89[c]
9[16]		20 min		90[c]
10[16]		20 min		92[c]
11		5 h, reflux	NR	

Table 1. (*Continued*)

Entry[a]	Epoxide	Time[b]	Product	Yield (%)
12		12 h, reflux	NR	
13		30 min	NR	

[a] Superscript against entry number refers to literature reference for the rearrangement product.
[b] All reactions were run at room temperature unless otherwise mentioned.
[c] Based on ^1H and ^{13}C NMR spectral analysis, the crude product was estimated to be >98% and hence it was not purified further.
[d] Refers to yield of isolated product after purification by Kugelrohr distillation or flash column chromatography.
[e] Ratio of products was determined by ^1H NMR analysis of the crude product.

be easily synthesized in the lab following a literature procedure.[11] The rearrangement does not require the use of an inert atmosphere or anhydrous solvent. The reagent is insoluble in common organic solvents and is used as a suspension. The catalyst is highly efficient and 0.1 mol% was sufficient to promote smooth rearrangement of most epoxides. For example, only 7 mg of the catalyst was needed to catalyze the rearrangement of 2 g of *trans*-stilbene oxide to diphenylacetaldehyde.[12] The catalytic efficiency of bismuth triflate was tested with styrene oxide as a model substrate. Remarkably, rearrangement of styrene oxide occurred even with as little as 0.01 mol% of bismuth triflate (15 mmol of styrene oxide, 1.5×10^{-3} mmol bismuth triflate). This fact makes this procedure especially attractive for large-scale synthesis. Dichloromethane was found to be the best solvent for the rearrangement. Rearrangement of *trans*-stilbene oxide using bismuth triflate was very slow in diethyl ether. In tetrahydrofuran, in addition to diphenylacetaldehyde, several unidentifiable byproducts were formed. When a solution of *trans*-stilbene oxide in dichloromethane was treated with 0.1 mol% of trifluoromethanesulfonic acid, the solution turned red and the resulting diphenylacetaldehyde was found to be considerably impure. This observation suggests that bismuth triflate is acting as a Lewis acid and not simply releasing triflic acid into the solution.

The rearrangement of *trans*-stilbene oxide (entry 1) proceeded with exclusive phenyl group migration to give diphenylacetaldehyde as the only product. Thus, this procedure is a good example of an epoxide rearrangement method that is both highly catalytic and regioselective in nature. In contrast, the rearrangement of *trans*-stilbene oxide by $MgBr_2$ in benzene gave a 3:1 mixture of diphenylacetaldehyde (phenyl migration) and deoxybenzoin (hydrogen migration).[2a] With $BF_3{\cdot}Et_2O$, *trans*-stilbene oxide gives only diphenylacetaldehyde while the *cis* isomer gives a mixture of diphenylacetaldehyde and deoxybenzoin.[2a] Rearrangement of *cis*-stilbene oxide (entry 2) with bismuth triflate gave a similar product mixture. It was found that hydrogen migrates in preference to a methyl group: both *cis*- and *trans*-β-methylstyrene oxides (entries 3 and 4) gave only phenylacetone upon rearrangement. Rearrangement of styrene oxide (entry 5) occurred readily and gave moderate yields of the acid sensitive compound phenylacetaldehyde. Aliphatic epoxides bearing a tertiary epoxide carbon also underwent rearrangement readily. For example, 1-methylcyclohexene oxide underwent ready rearrangement to give an 89:11 mixture of 2-methylcyclohexanone (migration of methyl group) and 1-methyl-1-cyclopentanecarboxaldehyde (migration of C–C bond), respectively. In contrast, rearrangement of 1-methylcyclohexene oxide with LiBr–HMPA in benzene gave 1-methyl-1-cyclopentanecarboxaldehyde as the major product (95%).[2b] Aliphatic epoxides lacking a tertiary epoxide carbon did not undergo rearrangement in the presence of bismuth triflate. Both cyclohexene oxide and 1,2-epoxyhexane were recovered unchanged, even when heated at reflux for 12 h. When cyclohexene oxide is heated with $InCl_3$, while no rearrangement occurs, the corresponding chlorohydrin is obtained in a good yield.[2d]

The rearrangement of epoxides bearing an electron-withdrawing group was also studied. Acyl-substituted epoxides (entries 7–10) underwent smooth rearrangement with exclusive migration of the acyl group. Thus, this method provides easy access to β-oxoaldehydes via rearrangement of epoxides. Epoxides bearing a cyano group (entries 11 and 12) or nitro group (entry 13) proved resistant to the reaction conditions and the starting epoxide was recovered in good yield in all cases. In contrast, when *trans*-β-methyl-β-nitrostyrene oxide is treated with $BF_3{\cdot}Et_2O$, a mixture of five different products is obtained.[13] In the presence of $InCl_3$, rearrangement accompanied by loss of the nitro group to give 1-chloro-1-phenyl acetone is observed.[2d]

In summary, this work demonstrates a new method for high-yielding, selective rearrangement of aromatic epoxides to carbonyl compounds using $Bi(OTf)_3$. Advantages of this method include the highly catalytic nature of the reagent, low toxicity and low cost of the Lewis acid catalyst, fast reaction rates and insensitivity of the Lewis acid to air and moisture.

Acknowledgements

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12. *Representative procedure*: A solution of *trans*-stilbene oxide (2.00 g, 10.2 mmol) in CH_2Cl_2 (20 mL) was stirred as $Bi(OTf)_3{\cdot}xH_2O$ (approximately 7 mg, 0.01 mmol) was added. After 20 min, the reaction mixture was diluted with 10 mL of CH_2Cl_2 and washed with saturated $NaHCO_3$ (10 mL) and saturated NaCl (10 mL). The organic layer was dried (Na_2SO_4) and the solvent removed on a rotary evaporator to yield 1.84 g (92%) of diphenylacetaldehyde that was determined to be >98% pure by ^1H and ^{13}C NMR spectroscopy.
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