

The Discovery-Oriented Approach to Organic Chemistry.7. Rearrangement of *trans*-Stilbene Oxide with Bismuth Trifluoromethanesulfonate and Other Metal Triflates

A Microscale Green Organic Chemistry Laboratory Experiment

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Epoxides, or oxiranes, are among the most versatile intermediates in organic synthesis (1). The inherent ring strain of epoxides makes them susceptible to a wide variety of reagents. A synthetically useful reaction of epoxides is their rearrangement to carbonyl compounds using Lewis acids. This rearrangement is a well-studied reaction that is commonly effected with the use of Lewis acids such as boron trifluoride etherate, magnesium bromide, zinc chloride, or tin(IV) chloride (2). We have previously described a discovery-oriented organic chemistry lab that illustrates the rearrangement of epoxides using $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (3). Some problems associated with boron trifluoride etherate—it is corrosive, toxic, and has a poor shelf life—make it unsuitable for use in an organic chemistry lab.

Although green chemistry principles (4) are increasingly stressed in the undergraduate curriculum, there are only a few lab experiments (5) wherein the toxicity of reagents is taken into consideration in the design of the experiment. In an effort to develop a microscale experiment illustrating epoxide rearrangement using environmentally benign catalysts, we initially focused on bismuth-based catalysts. In spite of its heavy metal status, most bismuth compounds are remarkably nontoxic and

easy to handle (6). For example, the LD_{50} values of most bismuth compounds suggest that they are even less toxic than sodium chloride (6a). Although the nontoxicity of bismuth compounds is fast earning bismuth metal the status of a green element, bismuth compounds are still not commonly used in organic synthesis. We have also extended this experiment to lanthanide salts, which have attracted considerable attention in organic synthesis owing to their relatively low toxicity, ease of handling, and water tolerance (7). Herein we report a discovery-oriented lab that illustrates the rearrangement of *trans*-stilbene oxide using a variety of metal triflates, where triflate is trifluoromethanesulfonate, CF_3SO_3^- (Table 1).

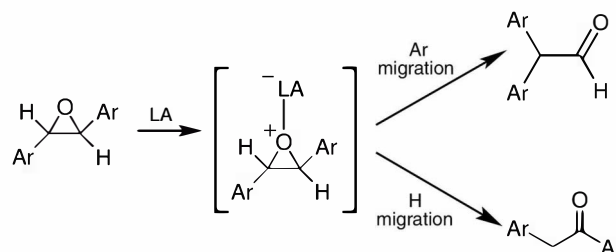
The element of discovery, which is introduced in the form of product identification using ^1H NMR spectroscopy, ensures that student interest and enthusiasm are retained. In addition to the discovery element, the experiments are carried out on a microscale with minimal or no workup, making them especially suitable for large laboratory sections. The experiment can be completed in less than ten minutes, allowing ample time for NMR analysis, even for a large laboratory section.

The identity of the product in an epoxide rearrangement depends on the nature of the migrating group and the direction of ring opening (Scheme 1). Two main factors that come into play are the inherent migratory aptitude of the group, as determined by its ability to stabilize the developing positive charge on the carbon at the transition state, and the ability of the group that is left behind to stabilize the transition state (8). A survey of the numerous examples found in the literature indicates that the relative migratory aptitude of the groups on the oxirane ring is aryl > H > alkyl. However, exceptions to this are known, and the position of hydrogen in this series is often unpredictable. The nature of the Lewis acid and the solvent also play a role in determining the course of the reaction (8).

Table 1. Rearrangement of *trans*-Stilbene Oxide Using Metal Triflates as Catalysts

Catalyst	Solvent	Major Product
$\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$	CH_2Cl_2	2
$\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$	CDCl_3	2
$\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$	CH_3CN	NR
$\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$	Diethyl ether	2
$\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$	THF	2
$\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$	Toluene	2
$\text{In}(\text{OTf})_3$	CH_2Cl_2	2
KOTf	CH_2Cl_2	NR
$\text{La}(\text{OTf})_3$	CH_2Cl_2	NR
$\text{La}(\text{OTf})_3$	CH_2Cl_2	NR

NOTE: OTf is trifluoromethanesulfonate, CF_3SO_3^- .



Scheme 1. Reaction showing the transition state and the possible products. LA is the Lewis acid.

Two possible products can result from the rearrangement of *trans*-stilbene oxide, **1**. Migration of the phenyl group will yield diphenylacetaldehyde, **2**, while migration of a hydride will result in formation of deoxybenzoin, **3**. We have carried out the rearrangement of *trans*-stilbene oxide in several solvents using a variety of metal triflates as catalysts. These results are summarized in Table 1.

The most efficient catalysts were bismuth triflate and indium triflate. In all cases, diphenylacetaldehyde (resulting from phenyl group migration) was the only product that could be detected by ¹H NMR spectroscopy. No rearrangement was observed using potassium triflate, lanthanum triflate, or ytterbium triflate as the catalyst. The rearrangement was very slow in CH₃CN while the use of diethyl ether and THF gave considerably impure product. The other possible product of the rearrangement, deoxybenzoin **3**, could not be detected by ¹H NMR spectroscopy in any case. When the rearrangement was carried out in CH₂Cl₂, diethyl ether, THF, or toluene the product was analyzed by removing the solvent using a stream of air and then dissolving the residue in CDCl₃. Subsequently, we found that the rearrangement works well in CDCl₃, eliminating the need for any work-up associated with the use of other solvents listed in Table 1. Acid-sensitive compounds such as diphenylacetaldehyde do, however, degrade with time in CDCl₃ and caution must be exercised if the spectra are not obtained within a few hours. We found that the product did not undergo any significant degradation in CDCl₃ over the course of 4 hours.

Experiment

¹H NMR spectra were recorded on a JEOL NMR spectrometer at 270 MHz. *trans*-Stilbene oxide was purchased from Aldrich Chemical Co. Metal triflates were purchased from Aldrich Chemical Co. and stored in a vacuum desiccator.

Hazards

Acetonitrile, chloroform-*d*, dichloromethane, diethyl ether, THF, and toluene vapor are irritants of the respiratory tract and hence they should be handled only in a well-ventilated area. Diethyl ether and THF are especially flammable and hence no flames should be present in the lab during this experiment. Although the metal triflates are not especially corrosive or toxic, skin contact should be avoided. Chloroform and dichloromethane are reasonably anticipated to be carcinogens. Toluene has been identified as a reproductive toxin.

Summary

A microscale discovery-oriented experiment illustrating the rearrangement of *trans*-stilbene oxide using non-corrosive metal triflates as catalysts has been developed. The use of CDCl₃ as the reaction solvent eliminates the need for any workup and avoids the use of highly toxic boron trifluoride etherate as a catalyst and additional reaction solvent.

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