

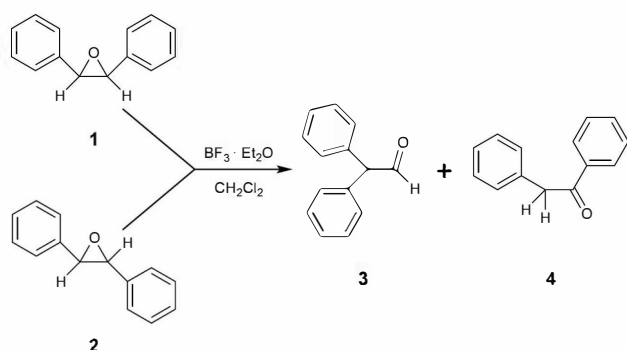
## The Discovery-Oriented Approach to Organic Chemistry. 3. Rearrangement of *cis*- and *trans*-Stilbene Oxides with Boron Trifluoride Etherate

An Exercise in  $^1\text{H}$  NMR Spectroscopy for Sophomore Organic Laboratories

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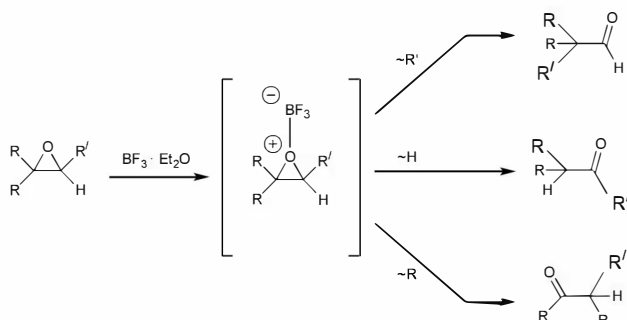
Epoxides, or oxiranes, are among the most versatile intermediates in organic synthesis (1). The inherent ring strain of epoxides makes them susceptible to a wide variety of reagents. Yet very few examples of experiments that illustrate the reactivity of epoxides can be found in lab texts (2). We have developed a simple discovery-oriented lab that illustrates the ease with which epoxides undergo rearrangements with Lewis acids. The added element of discovery ensures that students' interest and enthusiasm are retained.

The experiment involves the rearrangement of *cis*-stilbene oxide 1 and *trans*-stilbene oxide 2 with boron trifluoride etherate (Scheme I), analysis of the product by  $^1\text{H}$  NMR spectroscopy, and preparation of a crystalline derivative.



Scheme I

The rearrangement of epoxides to carbonyl compounds is a fairly well studied reaction. The reaction is commonly effected with the use of Lewis acids such as boron trifluoride etherate, magnesium bromide, zinc chloride, and tin(IV) chloride (3). The identity of the product depends on the nature of the migrating group and the direction of ring opening (Scheme II).



Scheme II

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 as well (4). A survey of the numerous examples found in the literature indicates that the relative migratory aptitude of the groups on the oxirane ring is  $\text{aryl} > \text{H} > \text{alkyl}$ . 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 considerable role in determining the course of the reaction (5).

Two possible products can result from the rearrangement of either *cis*-stilbene oxide 1 or *trans*-stilbene oxide 2. Migration of the phenyl group will yield diphenylacetaldehyde 3, while migration of a hydride will result in formation of deoxybenzoin 4. We have carried out the rearrangement of both *cis*- and *trans*-stilbene oxides with boron trifluoride etherate in both dichloromethane and diethyl ether as the solvent. A short reaction time (5 min) appears to be critical in obtaining pure product. The *trans*-stilbene oxide 2 gives diphenylacetaldehyde as the only product in either solvent, whereas the *cis*-stilbene oxide 1 gives ca. 7% of deoxybenzoin (migration of hydrogen) in diethyl ether and ca. 3–4% of deoxybenzoin in dichloromethane as the solvent. A small amount of other unidentifiable impurities can be seen in case of *cis*-stilbene oxide, but this does not interfere with product analysis. The identity of the product can be easily determined by  $^1\text{H}$  NMR spectroscopy, and in case of the *trans* isomer, by the determination of the melting point of the corresponding semicarbazone derivative as well.

It appears that the migratory aptitude of the phenyl group is much greater than that of the hydrogen in both isomers. Thus, the configuration of the epoxide must not be very important in determining which group migrates. The phenyl group can stabilize a developing positive charge at the adjacent carbon by way of a phenonium ion, and hence, it migrates preferentially to the hydrogen.

### Experimental Procedure

#### General Aspects

$^1\text{H}$  NMR spectra were recorded on a JEOL NMR spectrometer at 270 MHz. The *cis*- and *trans*-stilbene oxides were purchased from Aldrich Chemical Co. Boron trifluoride etherate was distilled from  $\text{CaH}_2$  and stored and dispensed from a dark-colored bottle capped with a septum.

## Safety

CAUTION: Dichloromethane vapor is harmful. It should be handled only in a well ventilated area. Diethyl ether and boron trifluoride etherate are highly flammable. Boron trifluoride etherate is toxic and air sensitive and should be dispensed in the hood. Semicarbazide hydrochloride is toxic and should be handled only with gloves.

## Rearrangement of *cis*- and *trans*-Stilbene Oxides

A solution of either *cis*- or *trans*-stilbene oxide (0.10 g, 0.51 mmol) in dichloromethane (4 mL) was stirred in a vial as boron trifluoride etherate (0.065 mL, 0.51 mmol) was added with a syringe. After 5 min, water (4 mL) was added, the mixture was stirred for 2 min, and the aqueous layer was removed with a pipet. The organic layer was washed with saturated aqueous NaCl (4 mL) and dried with sodium sulfate. The solvent was removed on a water bath maintained at 50–60 °C. Typical yields were 65 mg (65%). A drop of the product was used for <sup>1</sup>H NMR analysis. The remainder was used to prepare the semicarbazone derivative. <sup>1</sup>H NMR (CDCl<sub>3</sub>) For diphenylacetaldehyde δ 4.89 (d, 1H, *J* = 2.5 Hz), 7.30 (m, 10 H), 9.95 (d, 1 H, *J* = 2.5 Hz). Deoxybenzoin is detected by a singlet at δ 4.28 for its methylene group.<sup>1</sup>

## Preparation of Semicarbazone Derivative

A solution of semicarbazide hydrochloride (0.10 g) and anhydrous sodium acetate (0.225 g) in 4 mL of water was prepared. The product of rearrangement was dissolved in a minimum amount of ethanol (0.5 mL). Water was added until the solution turned turbid. The turbidity was cleared by dropwise addition of ethanol. This solution was then added to the semicarbazide solution and heated in a hot water bath for 15 min, during which time crystals formed. The mixture was cooled in ice, and the crystals (typical yield 50 mg) were collected by suction filtration and allowed to air dry. The melting point of the derivative from the *trans*-stilbene oxide rearrangement product was found to be 159–162 °C.<sup>2</sup>

## Acknowledgments

We wish to thank the students in the sophomore organic class at Illinois Wesleyan University for their enthusiastic participation in this discovery-oriented lab experiment, and Illinois Wesleyan University for providing research funds.

## <sup>w</sup>Supplemental Material

Supplementary material for this article is available in this issue of *JCE Online*.

## Notes

1. Both diphenylacetaldehyde and deoxybenzoin are commercially available and can be used to obtain reference NMR spectra.
2. The literature melting point of the semicarbazone of diphenylacetaldehyde is 162 °C and that of the semicarbazone of deoxybenzoin is 148 °C (6). The melting point of the semicarbazone derivative of *cis*-stilbene oxide rearrangement product was found to be 132–142 °C. Recrystallization did not change the melting point. The wide range indicates that a mixture of products is obtained in the rearrangement of *cis*-stilbene oxide.

## Literature Cited

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