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The Discovery-Oriented Approach to Organic Chemistry. 4. Epoxidation of p-Methoxy-trans- β -methylstyrene. An Exercise in ^1H NMR and ^{13}C NMR Spectroscopy for Sophomore Organic Laboratories

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The Discovery-Oriented Approach to Organic Chemistry.

4. Epoxidation of *p*-Methoxy-*trans*- β -methylstyrene

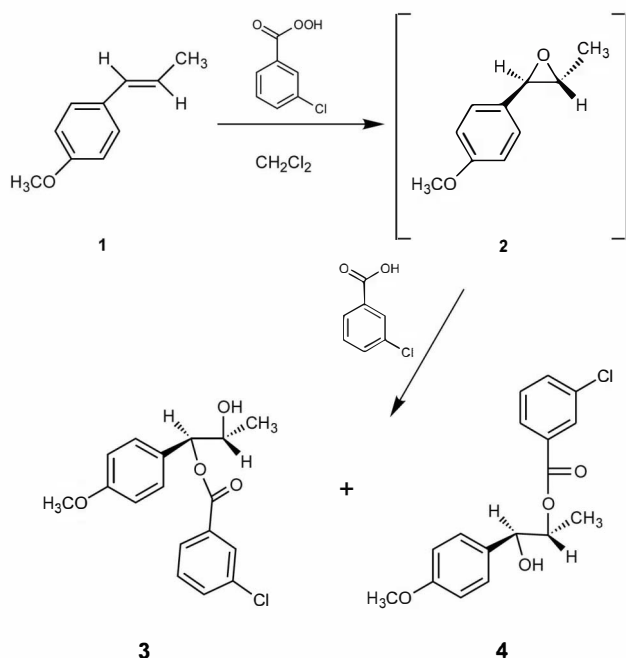
An Exercise in NMR and IR Spectroscopy for Sophomore Organic Laboratories

Rebecca S. Centko and Ram S. Mohan

Epoxidation of alkenes using peroxyacids is one of the most fundamental reactions in organic chemistry, yet there are very few examples of laboratory experiments that illustrate this important reaction (1). The inherent instability of many epoxides in acidic solutions makes the synthesis of acid-sensitive epoxides by this route difficult. Frequently, the carboxylic acid formed from the peracid during epoxidation reacts with acid-sensitive epoxides to give α -hydroxyesters as the major product. Procedures have been developed for epoxidation of alkenes in the presence of buffers to minimize this problem (2).

Overview of the Experiment

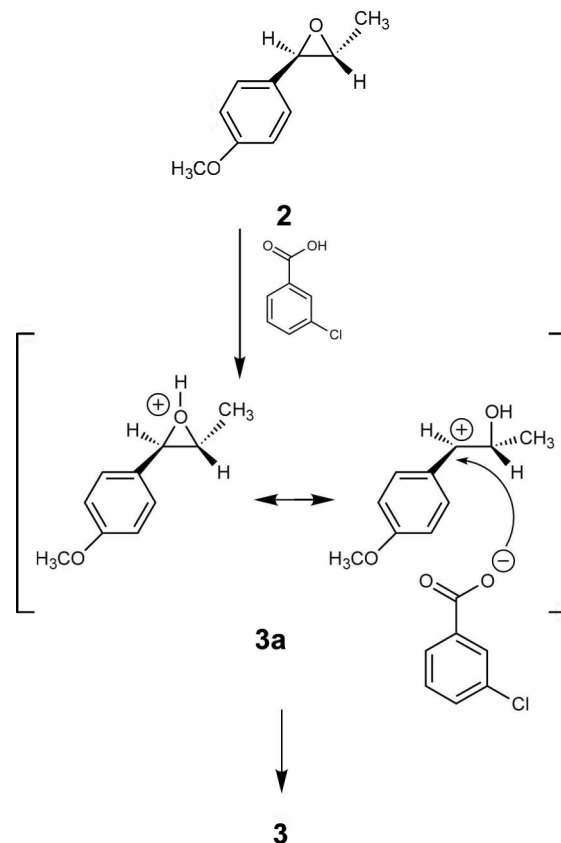
We have developed a discovery-oriented lab experiment that illustrates epoxidation of alkenes as well as the reactivity of epoxides toward acids. The added element of discovery ensures that students' interest and enthusiasm are retained. The experiment involves reaction of *p*-methoxy-*trans*- β -methylstyrene (*trans*-anethole) **1** with *m*-chloroperoxybenzoic acid (MCPBA), in both the absence and presence of a buffer. Owing to the reactivity of *trans*-anethole oxide, the expected epoxide **2** is



Scheme I

not formed in the absence of a buffer (Scheme I). Instead, the 3-chlorobenzoate ester **3**, resulting from ring opening of epoxide **2** by 3-chlorobenzoic acid, is produced in good yields. In the presence of sodium carbonate, epoxide **2** is formed in good yields. Products obtained are of sufficient purity to allow analysis by spectroscopy without further purification.

The identities of the products are conveniently determined by ^1H NMR, ^{13}C NMR, and IR spectroscopy. Each team consisting of two students carries out the epoxidation of *trans*-anethole, in both the absence and presence of a buffer. The entire reaction, including the work up, takes only about an hour. With the use of sufficient sample, both ^1H NMR and ^{13}C NMR spectra can be easily obtained in 15 minutes. Analysis of ^1H NMR, ^{13}C NMR, and IR spectra of the product obtained in the absence of a buffer indicates that the ester, which has been assigned structure **3**, is the major product.



Scheme II

Keywords: Second-year undergraduate, organic chemistry, inquiry-based discovery learning, IR spectroscopy.

The formation of **3** as the major product,¹ rather than **4**, can be attributed to a significant contribution to the resonance hybrid by the highly stable *p*-methoxy-substituted benzylic cation resonance form **3a** (Scheme II). This is consistent with the fact that in acid-catalyzed reactions, epoxides suffer attack at the carbon that can best stabilize positive charge (Scheme II).

The following are questions the students are expected to answer. Acceptable answers are also given.

- Are there peaks for epoxide hydrogens in the ¹H NMR spectra?

The expected epoxide ring hydrogen signals (δ 3–4) can be seen only in the product obtained in the buffered epoxidation.

- How many benzene ring carbons can be seen in the ¹³C NMR spectra?

The buffered reaction gives product that shows 4 benzene ring carbons, consistent with the expected epoxide. But the unbuffered reaction gives a product that shows 10 aromatic ring carbons. This suggests that the product contains 2 rings. Since the para substituted ring will only show 4 peaks, the other ring must be meta substituted to account for 10 peaks.

- Are there any other carbons in the ¹³C spectra? If so, what are the likely functional groups, on the basis of the chemical shift in the ¹³C NMR spectra?

The presence of an ester carbonyl is easily seen from the spectrum of the unbuffered reaction product.

- What functional groups are indicated by the IR spectra?

The IR spectrum of the unbuffered reaction product shows the presence of an OH group and also an ester carbonyl, suggesting the formation of a hydroxy ester.

- What is the theoretical yield of the product, assuming it is the epoxide? How does this compare to the observed yields?

The observed yield of product in the absence of buffer is almost twice the theoretical yield. This gives the first hint that the expected product has not formed. Rather, the higher mass recovery must be due to formation of a product with a much larger formula weight. Buffered epoxidation gives product in a yield comparable to the theoretical yield of the expected epoxide.

Experimental Section

General Aspects

¹H and ¹³C NMR spectra were recorded on a JEOL NMR spectrometer at 270 and 67.5 MHz, respectively. All chemicals used were reagent grade and were used as obtained. The concentration of MCPBA was determined by iodometric titration and was found to be 70% by weight.

Procedure A (No Buffer)

A solution of *trans*-anethole (0.50 g, 3.4 mmol) in CH₂Cl₂ (10 mL) was stirred and cooled in an ice bath as a solution of MCPBA (0.92 g, 3.7 mmol) in CH₂Cl₂ (10 mL) was added dropwise. The resulting mixture was stirred in the ice bath for an additional 20 min. The mixture was washed with 10% Na₂CO₃ (5 × 15 mL) and saturated NaCl solution (15 mL).² The organic layer was dried (Na₂SO₄) and the solvent was removed on a rotary evaporator³ to give 1.02 g (94%) of a

viscous oil. ¹H NMR (CDCl₃): δ 1.12 (3 H, d, *J* = 6 Hz, CHCH₃), 3.78 (3 H, s, COOCH₃), 4.2 (1 H, m, *J* = 7.2 Hz, 6 Hz, H_a), 5.72 (1 H, d, *J* = 7.2 Hz, H_b), 6.8–8.1 (4 H, m, ring protons). ¹³C NMR (CDCl₃) (15 peaks): δ 164.8 (C=O), 159.8, 134.6, 133.2, 131.9, 129.8, 129.7, 129.4, 128.6, 127.9, 114.1, 81.5, 70.2, 55.4, 18.9.

Procedure B (Buffered Epoxidation)

A biphasic mixture of a solution of *trans*-anethole (0.50 g, 3.4 mmol) in CH₂Cl₂ (10 mL) and 10% aqueous Na₂CO₃ solution (20 mL) was stirred well and cooled in an ice bath as a solution of MCPBA (1.4 g, 5.7 mmol, 1.7 equiv) in CH₂Cl₂ (20 mL) was added dropwise. After the addition was complete, the mixture was stirred for an additional 20 min in the ice bath. The organic layer was separated and washed with 10% aqueous Na₂CO₃ solution (5 × 25 mL) and saturated NaCl solution (15 mL). The organic layer was dried (Na₂SO₄) and the solvent was removed on a rotary evaporator to yield 0.52 g (95%) of a pleasant-smelling oil. ¹H NMR (CDCl₃): δ 1.42 (3 H, d, *J* = 5 Hz, CH₃), 3.04 (1 H, quartet of doublets, *J* = 5 Hz, 2 Hz), 3.52 (1 H, d, *J* = 2 Hz), 3.78 (s, OCH₃), 6.86 (2 H, d, *J* = 8.6 Hz), 7.17 (2 H, d, *J* = 8.6 Hz). ¹³C NMR (CDCl₃) (8 peaks): δ 159.6, 129.8, 126.9, 113.9, 59.5, 58.8, 55.3, 17.9.

Hazards

Dichloromethane vapor is harmful and inhalation should be avoided. MCPBA is shock sensitive and should not be ground in a mortar. The epoxide product has a pleasant but persistent odor and hence contact with skin and clothing should be avoided.

Acknowledgments

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Supplemental Material

Notes for the instructor and sample spectra are available in this issue of *JCE Online*.

Notes

1. Based on the ¹H NMR spectrum, there appears to be only one major product, which has been assigned structure **3** on mechanistic grounds. A smaller set of peaks also can be seen at δ 1.26 (d), 5.78 (d). Based on chemical shifts, these appear to be due to a small amount (<5%) of ester **4**, but overlapping signals do not permit accurate integration. GC-MS analysis of ester product did not show an M⁺ peak. The resulting fragments were not very characteristic and hence not useful in allowing structure determination. The ester carbonyl can also be clearly seen in the IR spectrum of **3**.

2. The excess peracid is removed by washing with 10% aqueous Na₂CO₃. The absence of peracid can be tested using starch–iodide paper.

3. Solvent can also be removed using a water bath maintained at 50 °C.

Literature Cited

1. For examples of epoxidation see Bradley, L. M.; Springer, J. W.; Delate, G. M.; Goodman, A. *J. Chem. Educ.* **1997**, *74*, 1336. Garin, D. L.; Gamber, M.; Rowe, B. *J. Chem. Educ.* **1996**, *73*, 555. Williamson, K. L. *Macroscale and Microscale Organic Experiments*, 2nd ed.; Heath: Lexington, MA, 1994; pp 300–303; epoxidation of cholesterol.
2. Mohan, R. S.; Whalen, D. L. *J. Org. Chem.* **1993**, *58*, 2663–2669. Svensson, A.; Ulf, L. M.; Somfai, P. *Synth. Commun.* **1996**, *26*, 2875–2880.