

Kinetic deuterium isotope effects on the reactions of 2-(4-methoxyphenyl)oxirane in water solutions

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This manuscript is dedicated to Professor James M. Coxon on his 65th birthday

Abstract

The rates of reaction of 2-(4-methoxyphenyl)oxirane (4-methoxystyrene oxide), *trans*-3-deutereo-2-(4-methoxyphenyl)oxirane and 3,3-dideutereo-2-(4-methoxyphenyl)oxirane in water solutions were measured as functions of pH. Kinetic deuterium isotope effects for the reactions of the mono- and di-deuterated (4-methoxyphenyl)oxiranes were determined for both the acid-catalyzed hydrolysis to diols and the pH-independent reactions leading mostly to rearranged aldehyde and involving a 1,2-hydrogen migration. The inverse kinetic deuterium isotopes for acid-catalyzed hydrolyses of the deuterated (4-methoxyphenyl)oxiranes to diols are consistent with rate-limiting epoxide ring opening. The magnitudes of the normal kinetic deuterium isotope effects on the pH-independent reactions of deuterated 4-methoxyphenyloxiranes are significantly smaller than the deuterium isotope effect on the aldehyde-forming step, and are rationalized by a reversible epoxide ring opening step that is partially rate-limiting. The magnitude of the partitioning isotope effect on the hydrogen migration step is consistent with isotope effects determined by Professor Coxon's laboratory on the Lewis acid-catalyzed rearrangements of deuterated phenyloxiranes in organic solvents.

Keywords: Phenyloxiranes, oxirane-carbonyl rearrangement, kinetic isotope effects

Introduction

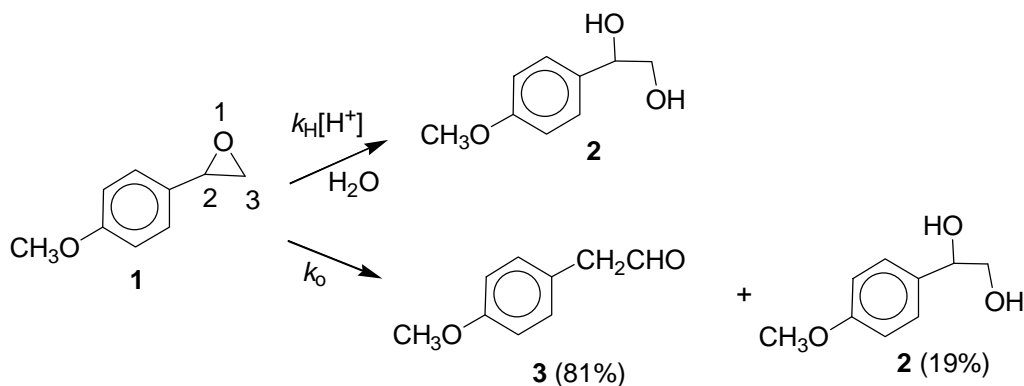
In the presence of Lewis acids, oxiranes (epoxides) often undergo rearrangement involving a 1,2-hydrogen migration to form aldehydes or ketones. In early work, for example, it was shown that BF₃ catalyzes the rearrangement of steroidal endocyclic epoxides to ketones^{1,2} and steroidal exocyclic epoxides to aldehydes.³ There are many other examples of BF₃-catalyzed oxirane-carbonyl reactions published in the literature. Solvents used for this reaction include benzene,

carbon tetrachloride and diethyl ether. Other Lewis acid/solvent reagents that catalyze the rearrangements of oxiranes to carbonyl compounds include LiBr-Bu₃PO/benzene,⁴ LiClO₄-Bu₃PO/benzene,⁴ LiBr-HMPA/benzene,⁵ LiBr/CH₃CN,⁶ Mo(CO)₆,⁷ 5.0 M LiClO₄/diethyl ether⁸ and Bi(OTf)·xH₂O/CH₂Cl₂.⁹

By studying the BF₃-catalyzed rearrangements of deuterium-labeled 2,2-dialkyl-substituted oxiranes in CCl₄, Blackett, Coxon, Hartshorn and Richards showed that there is a preference for migration of the C-3 hydrogen located trans to the more bulky group.¹⁰ This same group also studied the BF₃-catalyzed isomerization of 3-deuterio-2,2-dimethyloxirane, and concluded that the isotope effect (k_H/k_D) on the 1,2-hydrogen migration step is 1.9.¹¹ In another study of the BF₃-catalyzed rearrangement of an unsymmetrical 2,2-dimethyloxirane, a selective methyl migration in the rearrangement reaction was observed.¹²

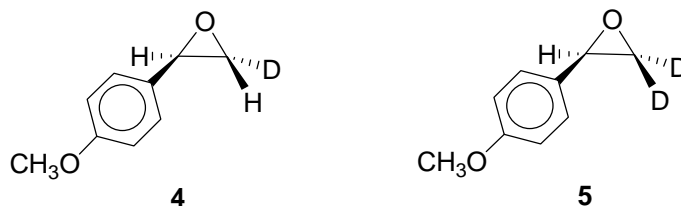
Acid-catalyzed hydrolysis of oxiranes generally yields diols from addition of water to the oxirane functionality. The reactivity of a given oxirane depends on the ability of substituent groups to stabilize positive charge on carbon. For example, the relative reactivity of methyloxirane, phenyloxirane and 2-(4-methoxyphenyl)oxirane toward acid-catalyzed hydrolysis is 1:45:1.8 x 10⁵, respectively.^{13,14} Addition of a water molecule and breaking of an oxirane C-O bond in the acid-catalyzed hydrolysis of methyloxirane are most likely concerted, whereas the mechanism of hydrolysis of 2-(4-methoxyphenyl)oxirane is stepwise via a carbocation intermediate.

At intermediate pH, where the concentration of H⁺ is sufficiently low, pH-independent or "water-catalyzed" reactions of many oxiranes are observed. These pH-independent reactions of simple oxiranes and sufficiently unreactive aryloxiranes also yield diol products, presumably from nucleophilic addition of a water molecule to the oxirane group. However, highly reactive oxiranes such as 2-(4-methoxyphenyl)oxirane,¹⁴ 5-methoxyindene oxide¹⁵ and 7-methoxy-1,2,3,4-tetrahydronaphthalene 1,2-epoxide¹⁶ undergo pH-independent reactions to yield primarily carbonyl compounds resulting from 1,2-hydrogen migration. This reaction is similar to the Lewis acid-catalyzed rearrangement of oxiranes to carbonyl compounds in aprotic, nonpolar solvents, and involves development of significant positive charge on carbon at the transition state. The polar water solvent stabilizes the transition state, in part by hydrogen bonding to the oxirane oxygen. Scheme 1 outlines the product-forming pathways for the reaction of 2-(4-methoxyphenyl)oxirane in water. Rate data for its reaction are given by $k_{\text{obsd}} = k_H[\text{H}^+] + k_o$, where k_H is the second-order rate constant for the acid-catalyzed reaction and k_o is the first-order rate constant for the pH-independent reaction.¹⁷ Thus, >99% of the reaction of **1** is acid-catalyzed at pH 4.5 and ~99% of the reaction of **1** occurs via the pH-independent pathway at pH 8.5. In the pH range 4.5-8.5, there is a changeover in mechanism from the acid-catalyzed pathway to the pH-independent pathway.



Scheme 1. Products from acid-catalyzed and pH-independent reactions of 2-(4-methoxyphenyl)oxirane.

We have synthesized *trans*-3-deutero-2-(4-methoxyphenyl)oxirane (**4**) and 3,3-dideutero-2-(4-methoxyphenyl)oxirane (**5**), and have compared their pH-independent rates with the pH-independent rate of 2-(4-methoxyphenyl)oxirane (**1**). The observed kinetic deuterium isotope effects and the relative rates of 1,2-hydrogen migration vs. 1,2-deuterium migration in the step leading to 4-methoxyphenylacetaldehyde (**3**) are summarized in this paper and compared to those of recent unpublished results from Coxon's laboratory for the Lewis acid-catalyzed isomerization of phenyloxiranes to phenylacetaldehydes in aprotic, nonpolar solvents.¹⁸



Results and Discussion

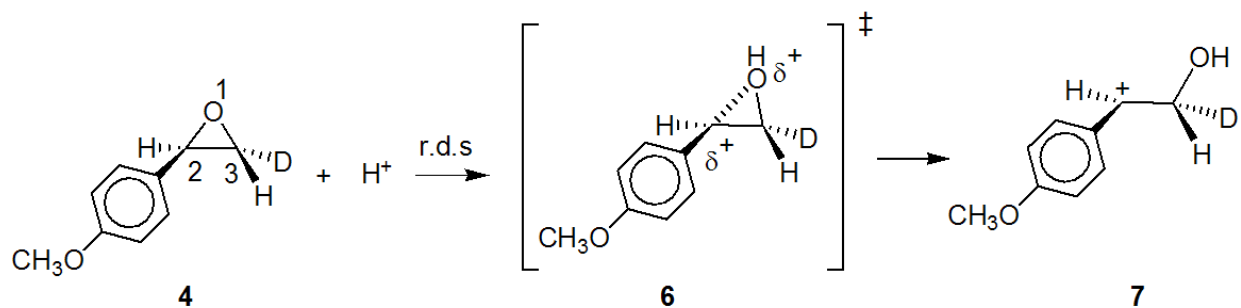
The rates of reaction of the parent methoxyphenyloxirane **1**, the *trans*-3-deuterium-substituted derivative **4** and the 3,3-dideutero-substituted derivative **5** were determined at pH ~5.3-5.4, where acid-catalyzed hydrolysis predominates, and at pH 8.5, where the pH-independent reaction predominates.¹⁷ Table 1 summarizes the observed kinetic isotope effects on the acid-catalyzed reaction ($k_{\text{H}}(\mathbf{1})/k_{\text{H}}(\mathbf{4})$ and $k_{\text{H}}(\mathbf{1})/k_{\text{H}}(\mathbf{5})$) and on the pH-independent reactions ($k_o(\mathbf{1})/k_o(\mathbf{4})$ and $k_o(\mathbf{1})/k_o(\mathbf{5})$).

Table 1. Kinetic deuterium isotope effects for acid-catalyzed and pH-independent reactions of mono-deuterated oxirane **4** and di-deuterated oxirane **5** in water, 0.1 M NaClO₄, 25.0 °C^a

$k_H(\mathbf{1})/k_H(\mathbf{4})$	$k_H(\mathbf{1})/k_H(\mathbf{5})$	$k_o(\mathbf{1})/k_o(\mathbf{4})$	$k_o(\mathbf{1})/k_o(\mathbf{5})$
0.97 ± 0.01^b	0.95 ± 0.01^c	1.17 ± 0.02^d	1.43 ± 0.01^e

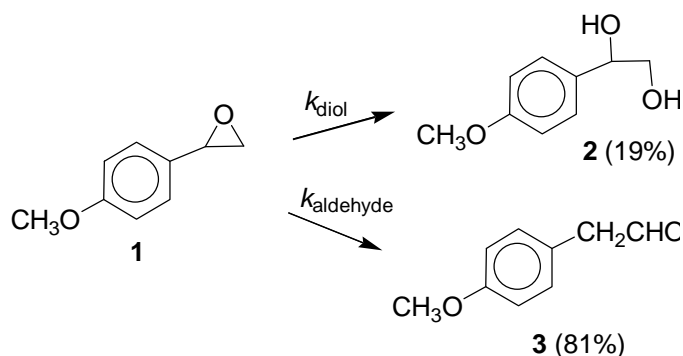
^aValues of k_H and k_o for reaction of **1** under these conditions are $1.1 \times 10^4 \text{ M}^{-1}\text{s}^{-1}$ and $3.0 \times 10^{-3} \text{ s}^{-1}$, respectively. ^bAverage of four independent measurements of k_H/k_D , two at pH 5.30 and two at pH 5.36. ^cAverage of two independent measurements of k_H/k_D at pH 5.39. ^dAverage of 11 independent measurements of k_H/k_D over the pH range 9.1-12.2. ^eAverage of four independent measurements of k_H/k_D , two at pH 8.7 and two at pH 9.2.

The slightly inverse kinetic deuterium isotope effect $k_H(\mathbf{1})/k_H(\mathbf{4})$ and slightly more inverse kinetic deuterium isotope effect $k_H(\mathbf{1})/k_H(\mathbf{5})$ on the acid-catalyzed hydrolyses of mono- and di-deuterated oxiranes **4** and **5**, respectively, are consistent with rate-limiting oxirane ring opening via transition state **6** to yield a carbocation intermediate **7**,¹⁹ which undergoes reaction with water solvent in a second step to give diol product (Scheme 2). Proton transfer to the oxirane oxygen must precede or be concerted with oxirane C–O bond breaking. The hybridization of the 3-carbon undergoes change from approximately sp^2 on the reactant epoxide to sp^3 in the intermediate carbocation **7**, and an inverse deuterium isotope effect on this step is expected. Two 3-substituted deuteriums give a slightly more inverse kinetic isotope effect than one 3-substituted deuterium. The inductive effect of deuterium may also contribute to the observed inverse isotope effect on k_H .

**Scheme 2.** Rate-determining step in the acid-catalyzed hydrolysis of **4**.

The pH-independent reaction of **1** is more complicated. The major product (81%) is 2-(4-methoxyphenyl)ethanal (**3**), but a significant amount of 1-(4-methoxyphenyl)-1,2-ethanediol (**2**, 19%) is also formed. In a study of the LiClO₄/diethyl ether-catalyzed isomerization of chiral cis-3- and trans-3-deuterated phenyloxiranes to 2-phenylethanal, Coxon and Nam have concluded 1) that rotation of the lithium-coordinated oxygen in the direction of the phenyl group is favored over rotation away from the phenyl group and 2) that hydrogen migration with deuterium remaining on the 3-carbon is favored over deuterium migration with hydrogen remaining on the

3-carbon by factors of 2.0 (for *trans*-3-deuterio) and 2.9 (for *cis*-3-deuterio).¹⁸ The isotope effect on the hydrogen migration step in the rearrangement of phenyloxirane catalyzed by lithium perchlorate in diethyl ether is therefore approximately 2-3, a value much larger than the kinetic deuterium isotope effects measured for the reactions of deuterated 4-methoxyphenyloxiranes **4** and **5**.

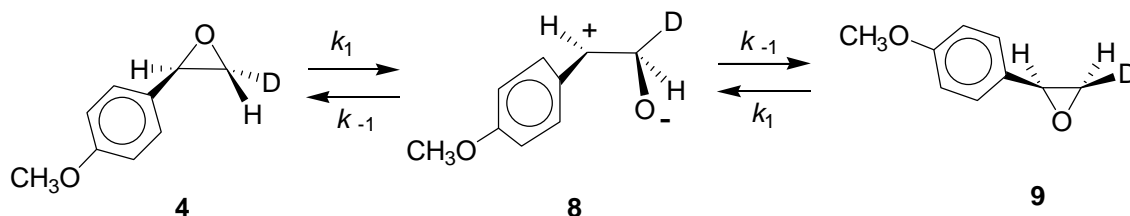


Scheme 3. Diol- and aldehyde-forming reactions in the pH-independent reaction of **1**.

From ¹H NMR analysis of the aldehyde formed in the pH-independent reaction of *trans*-3-deuterio-2-(4-methoxyphenyl)oxirane (**4**), the hydrogen/deuterium migration ratio was determined to be 2.9.²⁰ This ratio is slightly different from a deuterium isotope effect on 1,2-hydrogen migration, since hydrogen migrates leaving deuterium behind, instead of leaving hydrogen behind, in the aldehyde-forming reaction of **4**. Thus, secondary deuterium isotope effects are also incorporated into the H/D migration ratio for reaction of **4**. The secondary isotope effects are expected to be rather small, however, and the deuterium isotope effect on the hydrogen migration step is therefore much larger than the observed kinetic deuterium isotope effects on the pH-independent reactions of **4** and **5**. If it is assumed that **1** reacts to form aldehyde in a one-step reaction (k_{aldehyde}) and that diol **2** is formed by either concerted or stepwise mechanisms (k_{diol}), k_o would be equal to the sum of the rate constants leading to each product (Scheme 3 for reaction of **1**; $k_o = k_{\text{diol}} + k_{\text{aldehyde}} = 0.19k_o + 0.81k_o$). If it is further assumed that the deuterium isotope effect on the hydrogen migration step is 2.9 and that the deuterium isotope effect on the diol-forming reaction is unity (since only a small secondary isotope effect is expected), then the rate of the diol-forming reaction of **5** would be the same as that of **1**, and the rate of the aldehyde-forming reaction of **5** would be reduced by a factor of ~ 2.9 . Thus k_o for reaction of **5** is calculated to be less than half that of **1**, and a normal kinetic isotope effect of >2 is expected. However, the observed kinetic isotope $k_o(\mathbf{1})/k_o(\mathbf{5})$ is only 1.43, which is not consistent with a mechanism in which the aldehyde product **3** is formed in a one-step, concerted reaction from oxirane **1**.

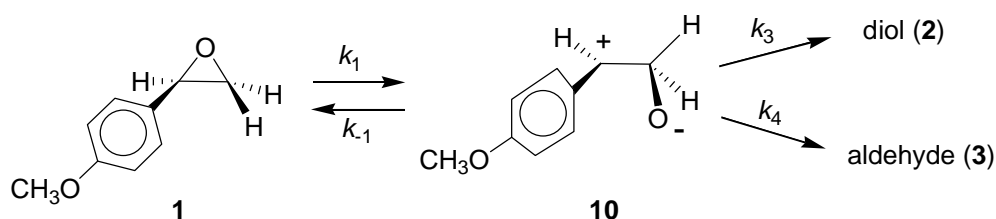
Yields of diol and aldehyde products from the pH-independent reaction of **1**, **4** and **5** have been determined, and the aldehyde/diol ratios are 81/19, 74/26 and 67/33, respectively. These

product ratios reflect deuterium isotope effects on the *product-forming* steps only, and are consistent with a deuterium isotope effect of ~2-3 on 1,2-hydrogen migration. A possible explanation for the observed kinetic deuterium isotope effects on the pH-independent reactions of **1**, **4** and **5** that are significantly smaller than the value of 2.9 for the hydrogen/deuterium migration ratio for reaction of **4** is given in Schemes 4 and 5.



Scheme 4. Isomerization of *trans*-deuterooxirane **4** and *cis*-deuteriooxirane **5**.

We previously observed that *trans*-3-deuterio-2-(4-methoxyphenyl)oxirane **4** undergoes isomerization to *cis*-3-deuterio-isomer **9** (Scheme 4) in competition with aldehyde- and diol-forming reactions during the course of its pH-independent reaction (Scheme 5).^{17,20} In order for this to happen, the benzylic C-O bond presumably breaks, and rotation about the C₂-C₃ bond occurs with the oxirane oxygen rotating either away from the aryl ring or toward the aryl ring. Rotation of this bond by 180°, followed by oxirane ring closure, yields the *cis*-3-deuteriooxirane **9**. Coxon and Nan have shown that rotation of the oxygen toward the phenyl ring in the isomerization of phenyloxirane in LiClO₄/diethyl ether solution is favored over its rotation away from the phenyl ring.¹⁸ The isomerization reaction may be either concerted, in which dipolar species **8** is a transition state, or stepwise, in which dipolar species **8** is a very short-lived intermediate. Observed kinetic deuterium isotope effects that are significantly lower than the deuterium isotope effect on the hydrogen migration step suggest that when **8** is formed from either **4** or **9**, it has a sufficient lifetime to partition both back to reactant epoxide and on to aldehyde product. Thus, the hydrogen migration step is only partially rate-limiting for the overall aldehyde-forming reaction.



Scheme 5. Stepwise mechanism for the pH-independent reaction of **1**.

$$k_0 = \frac{k_1(k_3 + k_4)}{(k_{-1} + k_3 + k_4)} \quad (1)$$

If **8** is regarded as a short-lived intermediate, then one of several kinetically equivalent mechanisms for reaction of **1** is given by Scheme 5. In this mechanism, both aldehyde and diol products are formed from the intermediate **10**. In other kinetically equivalent mechanisms, diol **2** is formed in a completely independent reaction pathway, either concerted or stepwise. The rate expression for the mechanism of Scheme 5 is given by equation 1. It has been reported that the rate constant (k_{isom}) for approach to an equilibrium mixture of **4** and **9** in 10:90 dioxane-water, starting from **4**, is ~ 3.4 times larger than k_o for reaction of **4**.²⁰ The value of $k_{-1}/(k_3 + k_4)$ will be different for **1**, **4** and **5** because of the deuterium isotope effect on the aldehyde-forming reaction. For the reaction of **4**, however, $k_{\text{isom}} \sim k_1$, and $k_{-1}/(k_3 + k_4)$ will have a value of $\sim 2-3$.²¹ Therefore, the aldehyde-forming step is not completely rate-limiting for the overall aldehyde-forming pathway, and not all of the isotope effect on the aldehyde-forming step will be reflected in k_o . Thus, the observed kinetic deuterium isotope effects $k_o(\mathbf{1})/k_o(\mathbf{4})$ and $k_o(\mathbf{1})/k_o(\mathbf{5})$ will be significantly smaller than either the partitioning isotope effect on hydrogen migration (~ 2.9) or the kinetic deuterium isotope effect calculated by the mechanism of Scheme 3 (~ 2.1).

Conclusions

The observed kinetic deuterium isotope effects (KIEs) for the pH-independent reactions of mono-deuterium-labeled 4-methoxyphenyloxirane (**4**) and di-deuterium-labeled 4-methoxyphenyloxirane (**5**) are 1.17 and 1.43, respectively. These observed KIEs are much smaller than the H/D migration ratio (2.9) in the aldehyde-forming pathway for reaction of **4**, and are also much smaller than the KIE value expected for reaction of **5** if the aldehyde product is formed from **5** in a concerted mechanism. The KIE values for reactions of **4** and **5** are consistent, however, with a stepwise mechanism via a dipolar intermediate **10** for the aldehyde-forming reaction. The deuterium isotope effect on the hydrogen migration step is fully expressed in determining the diol/aldehyde ratio, and measured aldehyde/diol ratios are consistent with deuterium isotope effect of close to 3 on the hydrogen migration step. However, the formation of the intermediate **10** is partially rate-limiting, and therefore the deuterium isotope effect on the hydrogen migration step is not fully expressed in the observed KIEs. Although diol **2** is possibly formed from intermediate **10**, it may also be formed from a completely independent reaction pathway via a carbocation intermediate.²²

Experimental Section

3-(4-Methoxyphenyl)-2,3-dibromopropanoic acid was prepared by the addition of bromine to *trans*-3-(4-methoxyphenyl)-2-propenoic acid in dichloromethane.²³ A solution of this dibromide in dichloromethane was stirred with solid sodium bicarbonate to yield *trans*-2-bromo-1-(4-methoxyphenyl)ethene free of its *cis* isomer.²⁴

***trans*-2-Deuterio-1-(4-methoxyphenyl)ethene.** For this preparation, a modified procedure of Neumann and Seebach was used.²⁵ A magnetically stirred solution of 10 mmol of *trans*-2-bromo-1-(4-methoxyphenyl)ethene in 42 mL of “Trapp-solvent” mixture (THF/Et₂O/pentane; 4:1:1) was cooled to -115 °C under nitrogen, and 20 mmol of *tert*-butyl lithium in pentane was added. The temperature of the reaction mixture was maintained at -115 °C for 1 h, and 20 mL of 99.9% deuterium oxide was added. The mixture was stirred and allowed to warm up to rt. The organic layer was washed with saturated sodium chloride solution, and the solvent was removed on a rotary evaporator to yield 1.13 g (86%) of *trans*-2-deuterio-1-(4-methoxyphenyl)ethene; ¹H NMR δ 5.56 (1 H, d, *J* = 17.6 Hz). A very small absorption at δ 5.10 (d, *J* = 10.5 Hz) indicated the presence of 1-4% of either 1-(4-methoxyphenyl)ethene or the *cis*-2-deuterio derivative. The exact amount of this minor contaminant varied slightly with the preparation. The temperature for this lithiation reaction is critical. If the temperature is only slightly warmer than -115°, acetylenic product is obtained.

***trans*-3-Deuterio-2-(4-methoxyphenyl)oxirane (4).** Various methods for epoxidation of *trans*-2-deuterio-1-(4-methoxyphenyl)ethene were attempted. The epoxide product is very reactive toward acidic reagents, and does not survive reaction conditions when the olefin is treated with peroxycarboxylic acids in dichloromethane solutions. Biphasic epoxidation of *trans*-2-deuterio-1-(4-methoxyphenyl)ethene with *m*-chloroperoxybenzoic acid/0.5 M NaHCO₃ solution²⁶ gave ~80% yield of oxirane product, but the *trans* oxirane **4** was contaminated with ~30% of the isomeric *cis*-deuteriooxirane (**9**). Slightly modified procedures often gave products other than the oxirane. Our best results were obtained by the epoxidation of *trans*-2-deuterio-1-(4-methoxyphenyl)ethene with peracetic acid that had been pretreated with sodium hydroxide to remove all traces of acetic acid. A solution of 0.40 g. (3.0 mmol) of *trans*-2-deuterio-1-(4-methoxyphenyl)ethene in 30 mL of dichloromethane was stirred with 4.0 g. of solid sodium carbonate at 0 °C, and 15 mL of 0.3 M peracetic acid (4.5 mmol) in dichloromethane, pretreated with crushed NaOH to remove the acetic acid, was slowly added over 3 h. The reaction mixture was stirred for an additional h. The solution was filtered, and the solvent was removed to yield *trans*-3-deuterio-2-(4-methoxyphenyl)oxirane (**4**) contaminated with ~10% of *cis*-3-deuterio-2-(4-methoxyphenyl)oxirane (**9**). The mass spectrum of this material indicated that > 99% of the (4-methoxyphenyl)oxirane product contained a single deuterium. Yields and purity of product varied greatly, depending on the amount of peracetic acid added, the rate at which it is added, and the rate at which the reaction mixture was stirred. On several occasions, yields of oxirane product were ~80%; ¹H NMR δ 2.77 (1 H, *J* = 2.6 Hz). A minor absorption at δ 3.09 (d, *J* = 4.2 Hz) indicated the presence of ~10% *cis*-3-deuterio-2-(4-methoxyphenyl)oxirane (**9**).

2,2,2-Trideutero-1-(4-methoxyphenyl)ethanone. A solution of 7.55 g. of 1-(4-methoxyphenyl)ethanone, 24.4 mL of triethylamine, 150 mL of THF and 100 mL of 99.9% D₂O was heated at 80 °C under nitrogen for 6 h. The reaction solution was cooled and extracted several times with ethyl acetate. The combined extracts were dried over anhydrous sodium sulfate, and the solvent was removed to yield 5.7 g. of 2,2,2-trideutero-1-(4-

methoxyphenyl)ethanone. ^1H NMR analysis of the product indicated that ~99% of the hydrogen at the methyl group had exchanged for deuterium.

3,3-Dideuterio-2-(4-methoxyphenyl)oxirane (5) was prepared from 2,2,2-trideutero-1-(4-methoxyphenyl)ethanone by the following sequence of known reactions: (1) reduction of 2,2,2-trideutero-1-(4-methoxyphenyl)ethanone with sodium borohydride in methanol to yield 2,2,2-trideuterio-1-(4-methoxyphenyl)ethanol, (2) conversion of 2,2,2-trideuterio-1-(4-methoxyphenyl)ethanol to 1-bromo-2,2,2-trideuterio-1-(4-methoxyphenyl)ethane with triphenylphosphite/bromine in CCl_4 ,²⁷ (3) treatment of 1-bromo-2,2,2-trideuterio-1-(4-methoxyphenyl)ethane with lithium carbonate in DMF to yield 2,2-dideuterio-1-(4-methoxyphenyl)ethene, (4) reaction of 2,2-dideuterio-1-(4-methoxyphenyl)ethene with bromine/ CH_2Cl_2 to yield 1,2-dibromo-2,2-dideuterio-1-(4-methoxyphenyl)ethane, (5) hydrolysis of the resulting dibromide in aqueous dioxane to yield 2-bromo-2,2-dideuterio-1-(4-methoxyphenyl)ethanol²⁸ and (6) reaction of 2-bromo-2,2-dideuterio-1-(4-methoxyphenyl)ethanol with powdered KOH/THF to yield di-deuteriooxirane **5**.¹⁶ The ^1H NMR spectrum of this product contained very minor doublets at δ 2.77 and 3.09, indicating the presence of ~1% of the trans deuteriooxirane **4** and ~1% of its cis deuterio isomer **9**.

Kinetic Procedures

For each kinetic run, approximately 5-10 μL of a solution of oxirane in dioxane (~10 mg/mL) was added to 2 mL of water solution in the thermostated cell compartment (25.0 ± 0.2 °C) of a UV-VIS spectrophotometer. The reaction solutions contained 0.1 M NaClO_4 and 10^{-3} M acetic acid buffer (for kinetic runs at pH ~ 5.3) or 10^{-3} M CHES (2-[N-cyclohexylamino]ethanesulfonic acid) buffer (for kinetic runs at pH ~9) to maintain constant pH throughout a given kinetic run. Reactions were monitored by UV detection at 230-235 nm. For isotope effect determinations, kinetic runs for non-deuterated and deuterated epoxides were run in the same solvent and staggered to minimize systematic errors. The half life of the spontaneous reaction of **1** under these conditions is ~4 min.

Product Studies

a) Acid-catalyzed hydrolysis of 1, 4 and 5. Solutions of 2-(4-methoxyphenyl)oxirane (**1**) and its mono- and di-deuterated derivatives **4** and **5** in dioxane (9-12 mg/mL) were prepared. An aliquot (20.0 mL) of each oxirane solution was added to 1.0 mL of 0.1 M NaClO_4 in which the pH had been adjusted to 4.0. The reaction solution was allowed to stand for ~1 min (> 10 half-lives for reaction), and the pH of the solution was adjusted to ~7 with 0.1 M NaOH solution. To this solution was added 20.0 mL of a solution of 5.8 mg of 4-methoxybenzyl alcohol in 1.0 mL methanol to serve as a standard for HPLC analysis. The resulting solution was analyzed by HPLC on a C_{18} reverse phase column with 40:60 methanol/water as the liquid phase, and products were detected by monitoring the effluent at 254 nm. At pH 4, $> 99\%$ of the reaction of each epoxide is acid-catalyzed, and only diol product is formed in each case. The HPLC

retention times of 1-(4-methoxyphenyl)-1,2-ethanediol (**2**) and 4-methoxybenzyl alcohol are 6.0 and 10.8 min, respectively.

b) pH-independent reactions of 1, 4 and 5. The exact procedure for reactions of oxiranes **1**, **4** and **5** at pH 4.0 were repeated except that the pH of the reaction solutions were adjusted to 8.5 and argon gas was bubbled through the reaction solutions before addition of the oxirane. After addition of each oxirane, the reaction solution was allowed to stand at rt for ~10 half-lives (0.75-1.0 h). An aliquot (20.0 mL) of the standard 4-methoxybenzyl alcohol in methanol was then added, and the solution was analyzed by HPLC under the conditions noted above. The total yield of diols at pH 8.5 was calculated by comparing the areas of the diol HPLC peaks relative to that of the standard 4-methoxybenzyl alcohol for reaction of each oxirane at pH 8 and at pH 4, and assuming that only diol was formed at pH 4. The reduction in yield of diols at pH 8.5 was assumed to be equal to the yield of aldehyde formed. The retention time of aldehyde product is 17.3 min, but this product decomposes slowly under these conditions, and calculation of aldehyde yield by comparison of its HPLC peak area with those of the diol peaks was considered unreliable.

Acknowledgments

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