196 *J. Org. Chem.* **1999,** *64,* 196−201

Experimental Investigation of the Primary and Secondary Deuterium Kinetic Isotope Effects for Epoxidation of Alkenes and Ethylene with *m*-Chloroperoxybenzoic Acid

Terry Koerner, H. Slebocka-Tilk, and R. S. Brown*

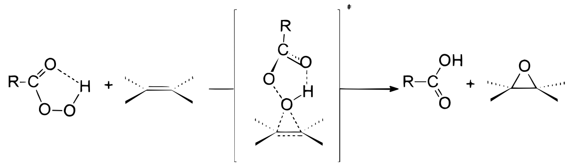
Department of Chemistry, Queen's University, Kingston, Ontario K7L 3N6, Canada

Received August 14, 1998

The secondary deuterium kinetic isotope effect (DKIE) for the epoxidation of ethylene and d_4-ethylene by *m*-chloroperoxybenzoic acid (MCPBA) is determined to be 0.83, or 0.95/α-H. The second-order rate constants for MCPBA and MCPBA-O-D epoxidation of a variety of alkenes that differ in the steric access to the double bond (*anti*-sesquinorbornene (**2**), tetramethylethylene (**3**), adamantylideneadamantane (**4**), 7-norbornylidene-7′-norbornane (**5**), bis(bicyclo[3.3.1.]non-9-ylidene) (**6**), bis(homoadamantane) (**7**), cyclohexene (**8**), 1-octene (**9**), *trans*-5-decene (**10**) and 2-methyl-1-pentene (**11**)) have been determined in dichloroethane at 25 °C using UV kinetics, and the primary DKIE, k_{OH}/k_{OD}, is 1.05 ± 0.05 in all cases. By comparison of the rates of epoxidation of sterically encumbered alkenes, it is suggested that the spiro epoxidation transition state is favored over a planar one. The products of the epoxidation of *anti*-sesquinorbornene are determined to be the epoxide and a *cis*-hydroxy ester, the latter most probably being formed by acid-catalyzed ring opening of the epoxide by in situ-produced *m*-chlorobenzoic acid produced in situ to form a *β*-hydroxy carbocation and carboxylate ion pair that collapses to product.

Introduction

The epoxidation of olefins with peracids is a familiar reaction and is generally thought to occur by a concerted mechanism originally proposed by Bartlett[1] in which the transition state has a "butterfly" configuration with symmetrical C−O bonding during oxirane formation. In 1975, Hanzlik and Schearer challenged the timing of C−O bond formation (eq 1) on the basis of results obtained from a deuterium kinetic isotope effect (DKIE) study of the reaction involving various deuterated isotopomers of *p*-phenyl styrene and *m*-chloroperoxybenzoic acid (MCPBA) at 0 °C.[2] The secondary DKIEs obtained for the d_2-*β*-carbon (0.82) and the d_1-α-carbon (0.99) of *p*-phenyl styrene prompted these authors to propose an unsymmetrical transfer of oxygen to the olefinic C's in the transition state for this reaction. Furthermore, on the basis of relative rates of different olefins, it was suggested that the unsymmetrical transition-state structure was not simply a consequence of the unsymmetric substitution of the alkene but rather a common occurrence in all olefins. This interpretation was supported by calculations at the STO-2G and STO-4G level[3] and more recently at the MP2/6-31G* level[4] for the reaction between ethylene and performic acid. By contrast, the results of a recent DKIE study of the reaction between MCPBA and the symmetrical alkenes 2,2,7,7-tetramethyl-*cis*-4-octene and its 4,5-di-d_2-isotopomer[5] and those from a combined theoretical and DKIE study of the reaction of MCPBA and 1-pentene[6] both suggest the mechanism involves a relatively symmetrical transition state with the spiro oxygen being roughly equidistant from the two olefinic carbons.

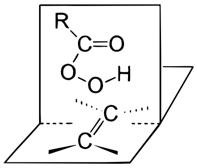
①  (1)

Because of its simplicity, ethylene has been used for many of the calculations involving secondary DKIEs accompanying various olefin reactions.[3,4,6−11] However, to our knowledge, no experimental evidence exists for the secondary DKIE accompanying epoxidation of this simplest olefin. Two other features of the epoxidation mechanism are also of interest, but little experimental information exists. The first concerns whether the approach of the peracid to the double bond occurs through a spiro (**1s**) or a planar (**1p**) transition structure (TS). All recent calculations indicate that the spiro TS is favored over the planar one, the preference being 5.1[11] and 3.7[12] kcal/mol for performic acid plus ethylene and *trans*-2-butene, respectively. Experimentally, this has been much more

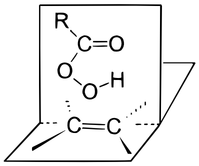
---

(1) Bartlett, P. A. *Rec. Chem. Prog.* **1957**, *18*, 111.
(2) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5231.
(3) Plesnicar, B.; Tasevski, M.; Azman, A. *J. Am. Chem. Soc.* **1978**, *100*, 743.
(4) Yamabe, S.; Kondou, C.; Minato, T. *J. Org. Chem.* **1996**, *61*, 616.
(5) Angelis, Y. S.; Orfanopoulos, M. *J. Org. Chem.* **1997**, *62*, 6083.
(6) Singleton, D. A.; Merrigan, S. R.; Liu, J.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 3385.
(7) Olson, L. P.; Niwayama, S.; Yoo, H.-Y.; Houk, K. N.; Harris, N. J.; Gajewski, J. J. *J. Am. Chem. Soc.* **1996**, *118*, 886.
(8) (a) Bender, R. B. *J. Am. Chem. Soc.* **1995**, *117*, 11239. (b) Bender, R. B.; Kubas, G. J.; Jones, L. H.; Swanson, J. E.; Capps, K. B.; Hoff, C. D. *J. Am. Chem. Soc.* **1997**, *119*, 9179.
(9) Koerner, T.; Brown, R. S.; Gainsforth, J. L.; Klobukowski, M. *J. Am. Chem. Soc.* **1998**, *120*, 5628.
(10) (a) Bach, R. D.; Glukhovtsev, M. N.; Gonzalez, C. *J. Am. Chem. Soc.*, in press. We thank Prof. Bach for a preprint of this work. (b) Bach, R. D.; Glukhovtsev, M. N.; Gonzalez, C.; Marquez, M.; Estevez, C. M.; Baboul, A. G.; Schelegel, H. B. *J. Phys. Chem. A* **1997**, *101*, 6092. (c) Bach, R. D.; Winter, J. E.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1995**, *117*, 8586.
(11) Houk, K. N.; Liu, J.; DeMello, N. C.; Condroski, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10147.
(12) We thank Prof. Bach for providing this number.

10.1021/jo981652x CCC: $18.00



1s

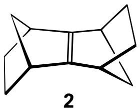


1p

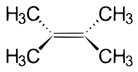
difficult to address because it is found that peracid epoxidation is quite insensitive to steric environments around the alkene.[13,14] Rebek[14] has cautiously suggested, both on the basis of his studies with U-shaped epoxidizing agents and for the reported[15] epoxidation of *anti*-sesquinorbornene (**2**) with MCPBA where anything other than a parallel TS is sterically constrained, that a parallel transition structure is favored for these systems. Nevertheless, he was careful to point out that this needed to be confirmed by extensive studies with other tetrasubstituted olefins.

Second, the timing of the intramolecular transfer of the proton from O−H to O=C in the peracid during epoxidation is of interest. As far as we know, there is only a single reported primary DKIE for peracid epoxidation of alkenes, that of $k_H/k_D = 1.17$ for the reaction of MCPBA plus *p*-phenyl styrene at 0 °C reported by Hanzlik and Schearer.[2] This number has been cited as evidence for an early transition state with little transfer of the H.[10] Nevertheless, this is a very unsymmetrical olefin and perhaps not representative of alkyl-substituted ones, so additional primary DKIE examples for peracid epoxidation of olefins of widely varying reactivity would cast light on the generality of that statement.

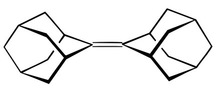
Herein, we report that the secondary DKIE for epoxidation of ethylene and ethylene-d_4 is $k_H/k_D = 0.83$, a value comparing favorably with that predicted by high-level computations.[6,10] In addition, to cast light on how the primary DKIE for epoxidation varies as a function of alkene reactivity, we have studied the kinetics of the reaction of MCPBA and MCPBA-O-D with a variety of aliphatic alkenes and found that this number ($k_{OH}/k_{OD} = 1.05 \pm 0.05$) is surprisingly insensitive to reaction rate and the nature of the alkene. Finally, we studied the kinetics of MCPBA epoxidation of alkenes **2**−**7**, cyclohexene (**8**), 1-octene (**9**), *trans*-5-decene (**10**), and 2-methyl-1-pentene (**11**), a series which has a wide variation in the accessibility of the epoxidizing agent to the double bond, in order to determine whether a spiro or planar TS is favored. The following describes the results of this study.



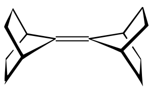
2



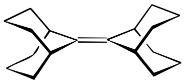
3



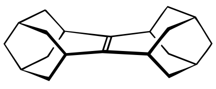
4



5



6



7

Experimental Section

Materials. Dichloromethane (4 L, Fisher, 99.9% ACS HPLC grade) was purified by heating to reflux for 24 h over CaH_2 followed by distillation; precautions were used to minimize moisture contamination during subsequent handling. 1,2-Dichloroethane (99.8%, HPLC grade, anhydrous, Sigma-Aldrich) was used without further purification.

Table 1. Secondary α-DKIEs for the Epoxidation of Ethylene with MCPBA in Dichloromethane at Ambient Temperature

% reaction	DKIE
62.5	0.833 ± 0.021[a]
84.1	0.815 ± 0.015
85.6	0.859 ± 0.016
96.8	0.808 ± 0.023
average	0.830 ± 0.012[b]

[a] Error computed as in ref 9, eq 4. [b] Standard deviation of the mean.

m-Chloroperoxybenzoic acid (Sigma-Aldrich, 57−80%) was purified by dissolving in dichloromethane and then washing with a phosphate buffer solution, pH 7.5.[16] *m*-Chloroperoxybenzoic acid-O-D was obtained by the procedure of Hanzlik and Shearer;[2] the deuterium content was found to be 95% by ^{1}H NMR.

Ethylene (Matheson of Canada Ltd., CP grade) and ethylene-d_4 (Merck Sharp & Dohme) were used without purification. 2, 3-Dimethyl-2-butene (**3**), cyclohexene (**8**), 1-octene (**9**), *trans*-5-decene (**10**) and 2-methyl-1-pentene (**11**, 99+%, Aldrich) were purchased and used without further purification. *anti*-Sesquinorbornene[17] (**2**, tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-2(7)-ene, or 1,2,3,4,5,6,7,8-octahydro-1,4;5,8-dimethanonaphthalene), adamantylideneadamantane[18] (**4**), 7-norbornylidene-7′-norbornane[19] (**5**), bis(bicyclo[3.3.1]non-9-ylidene)[20] **(6)** were made as described and had physical constants identical to those reported. 1,2,3,4,5,6,7,8,9,10,11,12,13,14-Tetradecahydro-1,5:3,7:8,12:10,14-tetramethanononalene (eicosene, bis(homoadamantane)[21,22] (**7**) was a gift from Professor Andrew Bennet, Simon Fraser University.

Kinetics. The kinetics of epoxidation were determined in dichloroethane at 25 °C under pseudo-first-order conditions of excess olefin by observing the rate of decrease in absorbance of MCPBA at 252 nm, $\epsilon_{252} = 18{,}600\ M^{-1}\ cm^{-1}$ in converting to MCBA, $\epsilon_{252} = 6{,}300\ M^{-1}\ cm^{-1}$. Kinetic measurements conducted at 284 nm (λ_{max}, $\epsilon_{max} = 15{,}200\ M^{-1}\ cm^{-1}$) and 293 nm were in excellent agreement with those at 252 nm. All solutions were prepared and stored under argon with protection from moisture.

For slower reactions, an OLIS (On-Line Instrument Systems, Bogart, Georgia) modified Cary 17 UV−vis spectrophotometer was used. Solutions containing the olefin in dichloroethane ($2-10 \times 10^{-3}$ M) were placed in a 3 mL quartz cuvette seated in the spectrophotometer cell holder for 15 min prior to kinetic measurements to allow thermal equilibration to 25 °C. Reactions were initiated by injection of 30 μL of a 1×10^{-2} M solution of MCPBA or MCPBA-O-D in dichloroethane into the contents of the cuvette. Pseudo-first-order rate constants (k_{obs}) were evaluated by fitting the absorbance vs time data to a standard exponential model via NLLSQ treatment. The reactions displayed excellent first-order kinetics. The k_{obs} used for determining the second-order rate constants given in Table 2, evaluated as $k_2 = k_{obs}$/[alkene], are the averages of 3−6 runs.

The faster rate constants were measured under pseudo-first-order conditions of excess olefin using stopped-flow kinetics (Applied Photophysics SX-17MX). Olefin concentration was varied from 2 to 7×10^{-3} M (after mixing), and the concentration of MCPBA (and its deuterated form) was varied from 1 to 2×10^{-4} M (after mixing). The stopped-flow k_{obs} used to

---

(13) Shea, K. J.; Kim, J.-S. *J. Am. Chem. Soc.* **1992**, *114*, 3044.

(14) Rebek, J.; Marshall, L.; McMannis, J.; Wolak, R. *J. Org. Chem.* **1986**, *51*, 1649.

(15) Bartlett, P. D.; Blakeney, A. J.; Kimura, M.; Watson, W. H. *J. Am. Chem. Soc.* **1980**, *102*, 1383.

(16) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1976**, *29*, 1976.

(17) Kopecky, K. R.; Miller, A. J. *Can. J. Chem.* **1984**, *62*, 1840.

(18) Flemming, M. P.; McMurry, J. E. *Org. Synth.* **1981**, *60*, 113.

(19) Bartlett, P. D.; Ho, M. S. *J. Am. Chem. Soc.* **1974**, *96*, 627.

(20) Keul, H. *Chem. Ber.* **1975**, *108*, 1207.

(21) Meijer, E. W.; Wynberg, H. *Tetrahedron Lett.* **1981**, 785.

(22) Watson, W. H.; Nagl, A. *Acta Crystallogr.* **1987**, *C43*, 2465.

Table 2. Second-Order Rate Constants and Primary DKIEs for Epoxidation of Various Olefins with *m*-Chloroperoxybenzoic Acid (k_2^H) and *m*-Chloroperoxybenzoic Acid-O-D (k_2^D) in Dichloroethane at 25 °C

olefin	k_2^H (M^{-1} s^{-1})	k_2^D (M^{-1} s^{-1})	k_2^H/k_2^D
ethylene	$(2.0 \pm 0.2) \times 10^{-5}$ [a]		
tetramethylethylene (**3**)	7.8 ± 0.2	7.4 ± 0.1	1.06 ± 0.03
cyclohexene (**8**)	$(7.1 \pm 0.2) \times 10^{-2}$	$(7.0 \pm 0.1) \times 10^{-2}$	1.01 ± 0.03
1-octene (**9**)	$(4.17 \pm 0.06) \times 10^{-3}$	$(3.98 \pm 0.04) \times 10^{-3}$	1.05 ± 0.03
trans−5-decene (**10**)	$(1.87 \pm 0.02) \times 10^{-2}$	$(1.86 \pm 0.03) \times 10^{-2}$	1.01 ± 0.03
2-methyl-1-pentene (**11**)	$(5.7 \pm 0.1) \times 10^{-2}$	$(5.5 \pm 0.1) \times 10^{-2}$	1.04 ± 0.03
anti-sesquinorbornene (**2**)	0.97 ± 0.03	0.90 ± 0.01	1.08 ± 0.04
adamantylideneadamantane (**4**)	84 ± 1	77 ± 2	1.08 ± 0.03
7-norbornylidene-7′-norbornane (**5**)	7.6 ± 0.1	7.2 ± 0.1	1.06 ± 0.04
bis(bicyclo[3.3.1]-non-9-ylidene (**6**)	12.8 ± 0.2	12.0 ± 0.3	1.06 ± 0.03
bis(homoadamantane) (**7**)	$(5.93 \pm 0.05) \times 10^{-3}$	$(5.56 \pm 0.05) \times 10^{-3}$	1.07 ± 0.03

[a] Second-order rate constant (k_2) was obtained by dividing the pseudo-first-order rate constant (k_{obs}), obtained from the GC integrations over time, by the concentration of peracid.

determine the second-order rate constants given in Table 2 are the averages of 10−12 runs. The primary DKIEs for the epoxidations (k_H/k_D) reported in Table 2 were determined by dividing the k_2^H for MCPBA by the k_2^D for MCPBA-O-D.

Product Studies. Approximately 20 mg of **2**, **4**, or **5** were dissolved in dichloromethane (50 mL), and a 10% excess of MCPBA was added in one portion. After approximately 10 half times, the reaction was quenched by adding 10 mL of an aqueous solution of 10% $NaHCO_3$ and 10% Na_2SO_3. The organic phase was washed with saturated NaCl and dried with $MgSO_4$. Solvent was removed by rotary evaporation, and the residue was submitted for IR and GC MS analysis. In the case of **4** and **5**, the corresponding epoxide was the only product. In the case of **2**, ^{13}C NMR analysis of the crude reaction mixture indicated that roughly 60% was epoxide and about 40% was the *cis*-1-hydroxy-2-(*m*-chlorobenzoate) ester of sesquinorbornene (**12**), identified by ^{13}C NMR, GC−MS, and IR analysis:^1H NMR (CD_2Cl_2) δ 7.95 (s, 1H), 7.88 (d, 1H), 7.58 (d, 1H), 7.40 (t, 1H), 5.35 (s, OH), 3.12 (s, 1H), 2.75 (s, 1H), 2.60 (s, 1H), 2.35 (s, 1H), 2.3−1.0 (remaining 12 H, complex pattern); ^{13}C NMR (CD_2Cl_2) δ 163.72 (C=O), 134.70, 133.30, 133.17, 130.17, 129.56, 127.88 (aromatic C's), 92.61, 84.69 (HO*C*-*C*OC(=O)Ar), 50.06, 46.34, 41.87, 41.13 (bridgehead), 38.92, 34.54 (methano CH_2), 24.99, 24.47, 23.96, 23.13 (ethano CH_2); electrospray MS 333.4, 335.4 (M^++ H); IR (KBr) 3536.7 (HO), 1717.6 (C=O) cm^{-1}.

DKIEs of Ethylene and Ethylene-*d*$_4$. The secondary DKIEs were determined using a competitive technique[23] in which approximately equal amounts of ethylene and ethylene-d_4 were incompletely epoxidized (60−97%) at ambient temperature. The fraction of reaction, initial isotopic ratio, and final isotopic ratios were determined by GC−mass spectrometric analysis (GC−MS). In a typical experiment, a solution was prepared by adding ethylene (0.1 mmol) and ethylene-d_4 (0.1 mmol) to a specially designed 50 mL vacuum line vessel containing degassed purified dichloromethane (45.0 mL). This was accomplished by monitoring the pressure in a vacuum line of known volume (74.77 mL) and then freezing the sample over the solvent using liquid nitrogen. Using a 2 mL gastight syringe, a sample of the ethylene stock solution (1.00 mL) was withdrawn and transferred into an evacuated vacuum line vessel. This vessel was attached to the vacuum line and its contents distilled into a flask containing bromine (0.5 mmol). After the ethylene had reacted, the remaining bromine was quenched using cyclohexene; an external standard of toluene was added, and the $BrCH_2CH_2Br/BrCD_2CD_2Br$ amounts were analyzed by GC−MS in order to determine the initial ethylene/ethylene-d_4 and total ethylene/toluene ratios. Purified MCPBA (2.0 mmol, a 10-fold excess) was added to the stock solution, and then aliquots were removed at appropriate times, brominated, and analyzed as above to determine the ethylene/ethylene-d_4 and total ethylene/toluene ratios. The analyses were performed on a Fisons Quattro mass spectrometer coupled to a Fisons GC 8000 gas chromatograph, HP-5 column, 30 m, 0.32 mm id, $T = 40$ °C, He carrier (2.0 psi). Each sample was subjects to 4−5 (0.2 μL) independent analytical runs. Quantitative evaluation was done by integration of the GC peaks attributable to the dibromoethylenes, and each isotope effect was confirmed by four independent experiments.

Results and Discussion

(i) Secondary DKIE for Reaction of MCPBA with Ethylene. Given in Table 1 are the secondary DKIEs for the epoxidation of ethylene and ethylene-d_4 in dichloromethane at ambient temperature. These were determined by mass spectrometric analysis of the brominated products of the unreacted alkenes in the reaction mixture following incomplete epoxidation of approximately equal amounts of ethylene and ethylene-d_4 in the same reaction vessel.[23] The method requires that the ratio of ethylene/ethylene-d_4 be exactly determined before and after expoxidation, which was accomplished by quantitatively transforming the residual olefins into 1,2-dibromoethane and dibromoethane-d_4, thereafter determining their amounts by GC integration (see Figure 1). In addition to the ethylene/ethylene-d_4 ratios, the extent of epoxidation is also required for this competitive technique and was determined from the ratio of total ethylene to an internal standard (toluene). The DKIE is calculated using eq 2,

$$\text{kie} = k_H/k_D = 1 + \left(\log\left[\frac{R_f}{R_0}\right]\Big/\log\left[(1 - f)\frac{(1 + R_0)}{(1 + R_f)}\right]\right) \quad (2)$$

where R_0 and R_f are the ethylene/ethylene-d_4 ratios initially and after some fraction, *f*, of expoxidation, respectively. The errors for the individual kie's were calculated by propagation of error as described.[9]

The data in Table 1 give an average secondary DKIE of 0.830 ± 0.012, or 0.95/α-D, associated with the epoxidation of ethylene. This is consistent with a rate-limiting transition state for the expoxidation where there is some modest, but unspecified, rehybridization of the olefinic carbons.[24,25] The inverse DKIE can be compared with that found recently for the bromination of ethylene of $k_{H4}/k_{D4} = 0.57-0.66$, shown by computations to be dominated by the creation of an new vibrational mode in the TS, termed the CH_2-symmetric twist, that arises from the loss of

---

[23] Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15.

[24] Streitwieser, A., Jr.; Jagow, R. H.; Fahey, R. C.; Suzuki, S. *J. Am. Chem. Soc.* **1958**, *80*, 2326.

[25] (a) *Isotope Effects in Chemical Reactions*; Collins, C. J., Bowman, N. S., Eds.; ACS Monograph 167, Van Nostrand Reinhold Co.: New York, 1970. (b) Westaway, K. C. In *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol. 7 pp 275−392. (c) Lowry, T. H.; Richardson, T. H. In *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; pp 232−234.

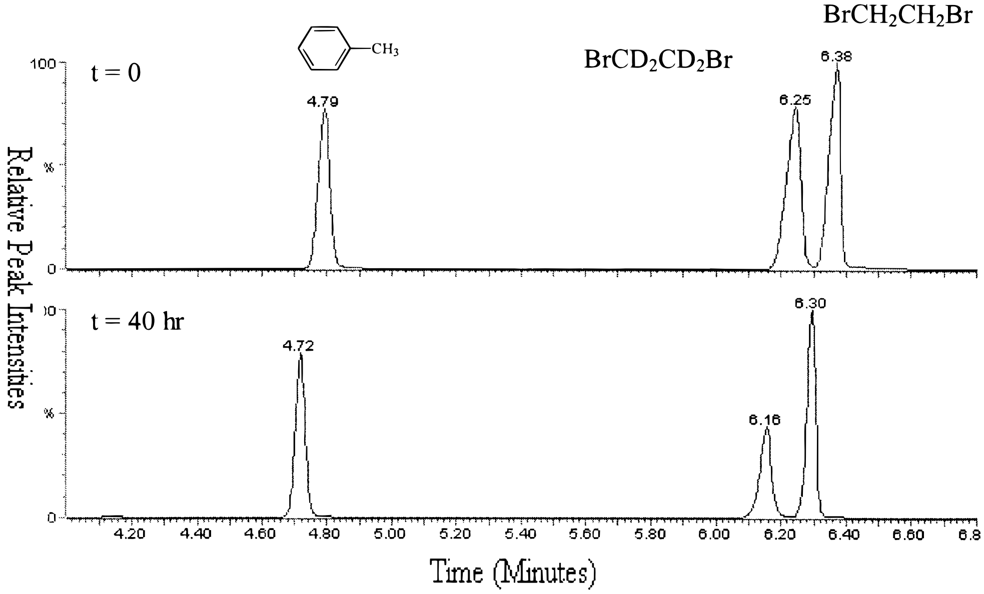


Figure 1. A typical chromatogram for the analyzed products of reaction of ethylene and d_4-ethylene with Br_2 obtained at time zero and some fraction of reaction with MCPBA (see Experimental Section).

rotational freedom about the C=C axis of ethylene.[9] It is also interesting to note that the value of 0.95/α-D is consistent with results obtained for other systems, in particular the epoxidation of the unsymmetrical olefin 1-pentene, where the DKIE for each of the two terminal α-C-Ds is 0.96−0.98, whereas that for the C_2-D is 0.93.[6] The ethylene and 1-pentene α-DKIEs are marginally higher than the 0.90 ± 0.03/α-CD reported by Angelis and Orfanopoulos[5] for the epoxidation of the symmetrical olefin 2,2,7,7-tetramethyl-4-*cis*-octene, but this number was determined using standard ^{1}H NMR and might not be as precise as those above. Houk et al.[6] have calculated at the B3LYP/6-31G* level that the transition state for epoxidation of propylene is nearly symmetrical with respect to the developing C−O distances, and the computed DKIEs for this system are 0.95/terminal C-D, and 0.93 for the C_2-D, consistent with the experimental result with 1-pentene. A symmetrical TS is also computed for ethyene,[11,10a] but to our knowledge, the computed secondary DKIE at the B3LYP/6-31G* level is not published. Nevertheless, our present ethylene secondary DKIE experimental data alone do not allow one to say much about the symmetry of the transition state and high-level computations are necessary to determine the transition structure for its epoxidation.

(ii) Kinetics of Reaction of Tetrasubstituted Alkenes with MCPBA and the Primary DKIE. The kinetics for epoxidation of alkenes with peracids previously have been studied using varied and somewhat labor-intensive methods. Among the most common were titration of the residual peracids,[26] proton NMR,[5,27] and gas chromatography,[2,13] but unfortunately none of these can provide precise constants, particularly those needed for accurate determination of secondary DKIEs. Recently, a new and highly precise NMR method for determining KIEs has been introduced by Singleton and co-workers,[28] and this methodology has been successfully used to determine the secondary DKIE for the reaction of MCPBA with the unsymmetrical olefin 1-pentene.[6]

The change in the UV spectrum that accompanies conversion of a peroxybenzoic acid to its corresponding benzoic acid turns out to be a very convenient and accurate tool for monitoring these reactions, being particularly valuable for determination of fast reaction rates and kinetic isotope effects. The epoxidations in the present study were run at 25 °C in dichloroethane under pseudo-first-order conditions of excess olefin and were found to be first order in both [olefin] and [MCPBA]. Given in Table 2 are the second-order rate constants for MCPBA epoxidation of olefins **2**−**11**, along with the values for epoxidation by MCPBA-O-D. The usual trend[2,26] in alkene reactivity was observed, namely that successive substitution of the double bond with alkyl groups enhances the rate of epoxidation. Where direct comparisons can be made, the results obtained here are in good agreement with kinetic data reported for epoxidation of aliphatic olefins with peracetic acid in acetic acid[26] and MCPBA in halogenated solvents.[13,29,30]

To our knowledge, the only experimental data concerning a primary DKIE for epoxidation of alkenes by peracids concerns the reaction of MCPBA with *p*-phenylstyrene (1.17 at 0 °C).[2] To obtain a clearer picture, we wanted to see if the primary deuterium KIE depends on symmetry, reactivity, and extent of substitution at the double bond. The observed primary DKIEs for the olefins in Table 2 are small (1.05 ± 0.05 at 25 °C) and effectively the same for all compounds, even though the second-order rate constant changed by roughly 4 orders of magnitude, i.e., from 4×10^{-3} M^{-1} s^{-1} for 1-octene (**9**) to 84 M^{-1} s^{-1} for adamantylideneadamantane (**4**).

There are several factors that could account for the insensitivity and small size of the observed primary DKIEs. It has been shown that peracids form intramolecular hydrogen-bonded species in dilute solutions of inert solvents, i.e., benzene, carbon tetrachloride, and

---

[26] Swern, D. *J. Am. Chem. Soc.* **1947**, *69*, 1692.

[27] Angelis, Y.; Zhang, X.; Orfanopoulus, M. *Tetrahedron Lett.* **1996**, *37*, 5991.

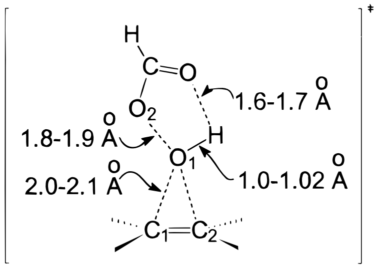
[28] Singleton, D. A.; Thomas, A. A. *J. Am. Chem. Soc.* **1995**, *117*, 9357.

[29] Kropf, H.; Yazdanbachsch, M. R. *Tetrahedron* **1974**, *30*, 3455.

[30] Andersen, L.; Berg, U.; Pettersson, I. *J. Org. Chem.* **1985**, *50*, 493.

dichloromethane.[31] The H-bonding to the carbonyl oxygen of the peracid would have the effect of lowering the difference in the vibrational zero point energies for the O−H and O−D bonds in the ground state, which in turn lower the primary DKIE. If the intramolecular hydrogen bond were maintained in the TS, as is customarily considered for the concerted epoxidation mechanism in eq 1, it would result in a nonlinear transfer of the hydrogen. Primary DKIEs for hydrogen transfers proceeding through bent transition states are both small and relatively insensitive to changes in transition structure.[32] The low and surprisingly consistent primary DKIEs observed for all the alkenes in Table 2 is in consonance with this interpretation.

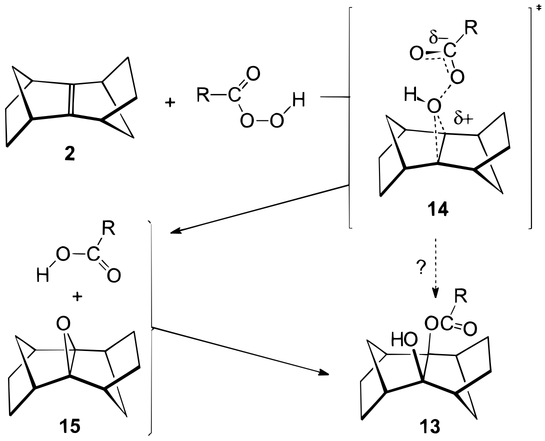
Alternatively, recent high-level computations of the performic acid epoxidations of a variety of simple alkenes[10−12] consistently indicate that the transition structure (**12**) involves association of the C_1 and C_2 carbons with the O_1−H oxygen, a lengthening of the O_1−O_2 bond, and a concomitant shortening of the O_2−C toward the carbonyl bond distance, but the O_1−H bond is only slightly elongated relative to that in performic acid. The transition structures for unsymmetrically substituted olefins such as propene have highly asynchronous C_1−OH and C_2−OH distances at the MP2 level, but at the B3LYP level,[6] the substituent induces only a small asynchrony, the latter two distances varying by about 0.1 Å. Bach[12] has suggested that there is minimal rehybridization of the ethylene at the TS and that the developing carboxylate anion is both resonance-stabilized and "ideally poised to accept the migrating H *after the transition barrier is crossed*." Because the hydrogen is transferred after the rate-limiting step, it is expected, and observed, that there is a small primary DKIE for peracid epoxidation.



12

(iii) Products of Reaction of MCPBA + *anti*-Sesquinorbornene (2). Epoxidation of *anti*-sesquinorbornene (**2**) with 3 equiv of MCPBA in CH_2Cl_2 was reported by Bartlett and co-workers[15] to produce the corresponding epoxide, which was purified by preparative GC with no yield given. In the present study, when the MCPBA epoxidation is conducted in $ClCH_2CH_2Cl$ under pseudo-first-order conditions of excess **2** (10^{-3} M, vs 10^{-4} M MCPBA), a clean reaction is observed spectrophotometrically. No precipitates are observed during the reaction at these concentrations. When the reaction is done preparatively at 10^{-3} M in each component, the initial product mixture comprises precipitated MCBA, epoxide (∼60%), and ∼40% of a material that proves to be the *cis*-hydroxy ester **13**, identified by MS, IR, and ^{1}H and ^{13}C NMR. In preparative runs containing equimolar **2** and MCPBA, monitored by ^{1}H NMR, the initial product ratio is stable for at least 30 min but on standing overnight the epoxide reacts slowly with the precipitated *m*-chlorobenzoic acid to produce the hydroxy ester. Given in Scheme 1 is a mechanism that accommodates these facts. It is based largely on the computational TS (**12**) suggested by Bach and co-workers where the transition structure resembles a distant association of the olefin with $HO^{\delta+}$, the latter separating slightly from $^{\delta-}OC(=O)R$. The structure of *anti*-sesquinorbornene does not readily allow the peracid to approach from the computationally favored spiro orientation, and most likely, the TS resembles a planar configuration as in **14** (C−OH−C distances not necessarily equal).

Scheme 1. Proposed Pathway for Epoxidation of *anti*-Sesquinorbornene, R = *m*-ClPh



Collapse to the epoxide (**15**) and *m*-chlorobenzoic acid occurs via the abstraction of the O-**H** by the developing encounter pair-carboxylate. It might be tempting to suggest that the formation of **13** early in the reaction arises from a second channel for collapse of the TS, but the available information is not conclusive given the formation of precipitates. More probably, **13** arises by reaction of the epoxide with nascent solubilized MCBA by an acid-catalyzed opening of the epoxide followed by ion pair collapse, and this process is retarded once the precipitation of the acid commences. The ionic opening of the three-membered ring leading to cis products has precedence, at least in the bromination of **2** in methanol, which we have shown leads to a 1/9 mixture of *cis*-dibromide to *cis*-methoxy bromide, the ratio being unaffected by the presence or absence of added Br^-.[33] In that example, although the symmetrical bromonium ion is almost certainly formed early in the reaction, it cannot lead to stable products unless it opens to an α-bromo carbocation, which then suffers ion pair collapse or solvent capture.

The fact that the epoxide in the initial product mixture slowly is transformed into the hydroxy ester in the presence of precipitated MCBA indicates that the overall process is subject to thermodynamic control. MMX calculations[34] of the total heats of formation of **2** + MCPBA (35.75 + −37.65 kcal/mol) → **15** + MCBA (3.43 + −68.89 kcal/mol) → **13** (−75.3 kcal/mol) indicate that the hydroxy ester is the thermodynamically most stable product for this reaction.

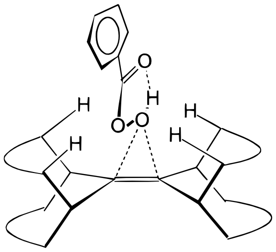
---

[31] (a) Giguere, P. A.; Olmos, A. W. *Can. J. Chem.* **1952**, *30*, 821. (b) Swern, D.; Witnauer, L. P. *J. Am. Chem. Soc.* **1955**, *77*, 5537.

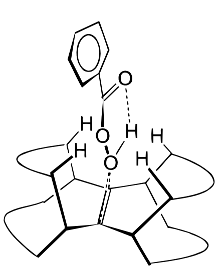
[32] More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 785.

[33] Slebocka-Tilk, H.; Gallagher, D.; Brown, R. S. *J. Org. Chem.* **1996**, *61*, 3458.

(iv) Spiro vs Planar Transition States. Although nonhindered **3** can accommodate either a planar or spiro TS, tetrasubstituted olefins **4**−**6** cannot accommodate a planar TS without strain because of the steric bulk at the ends of the double bond that interferes with the O-O-H moiety. For these olefins, a perpendicular TS minimizes the buttressing between the incoming MCPBA and alkene. MMX calculations[34] indicate that the H-H separations between the inward facing homoallylic hydrogens above the double bond in **4**, **5**, and **6** are 3.61, 3.87, and 3.33 Å respectively, and their distances from the nearest olefin carbon are 2.75, 2.76, and 3.01 Å. Assuming that the high level computations on performic acid plus ethylene (see structure **12**)[10−12] can be extrapolated to these systems, with some modest rehybridization of the C═C unit in the TS, the approaching peroxy oxygen would fit nicely into a perpendicular cleft formed by the homoallylic H's above the double bond as in **16**.



16



17

The fact that the rates for tetramethylethylene and these three tetrasubstituted olefins are within a factor of 10 indicates that there cannot be much steric hindrance to the epoxidation and that the spiro TS is favored. Conversely, olefins **2** and **7** place the homoallylic H's above and perpendicular to the double bond, with the respective H−H distances being 3.2−3.3 and 2.9 Å and the H−olefinic C distances being 2.6−2.7 Å. The clefts formed by the homoallylic H's in these molecules are clearly narrower than those in **4**−**6** and, with modest rehybridization of the C═C unit in the TS, would accommodate a planar transition structure for epoxidation, as in **17**, better than a symmetrical spiro one. The preference for the spiro transition state is probably reflected in the observed reduced rates of epoxidation for **2** relative to **5** and **6**, or **7** relative to **4**, although it is difficult to factor out all the kinetic consequences of the narrower clefts which may bias the interpretation. At best, we can say that the currently available experimental evidence supports a lower energy for the spiro TS than the planar one for these epoxidations. This is in agreement with the predictions made by calculation and in contradiction of the previous suggestion[14] of a favored planar TS made on the basis of limited examples.

Conclusions

The above study provides an experimental value for the secondary DKIE for the epoxidation of ethylene and ethylene-d_4 by MCPBA. The relatively low value of $k_{\mathrm{H4}}/k_{\mathrm{D4}} = 0.83$ (0.95/α-C-D) is consistent with a transition state where the olefinic carbons have undergone a small degree of rehybridization and is in agreement with the results obtained for the epoxidation of 1-pentene and with predictions made by high-level computations.[6]

UV kinetic studies of the epoxidation of a variety of alkenes by MCPBA and MCPBA-O-D indicate that a small normal primary DKIE of 1.05 ± 0.05 is observed for all the investigated examples which vary by a factor of over 10^4 in reactivity. The most satisfying explanation for the small value of the primary DKIE is that the rate-limiting step involves very little change in the bonding of the peroxyacid O−H bond, consistent with predictions made by high-level computations.[10−12] Finally, study of the kinetics of epoxidation of tetrasubstituted alkenes where the structures hinder one or the other of a planar or spiro transition state for epoxidation suggest that the latter is favored.

Acknowledgment. The authors gratefully acknowledge the financial assistance of the Natural and Engineering Research Council of Canada and Queen's University. In addition, they are grateful to Professor Andrew J. Bennet, Simon Fraser University, Burnaby, British Columbia for a generous gift of olefin **7** and to Professor R. D. Bach for stimulating discussions and a preprint. T.B.K. would like to thank Professor J. Stone, Queen's University, Kingston, Ontario for stimulating discussions about the MS analysis.

JO981652X

---

(34) Calculated with the PCMODEL for Windows program, Version 5.1 (Serena Software, Box 3076, Bloomington, IN 47402-3076).