6492 J. Am. Chem. Soc. 1988, 110, 6492-6497

A Mechanistic Characterization of the Spontaneous Ring Opening Process of Epoxides in Aqueous Solution: Kinetic and Product Studies[1]

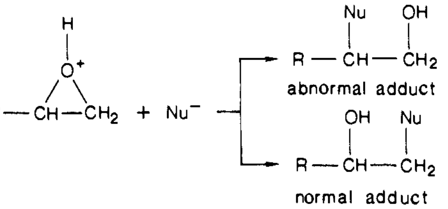
Y. Pocker,* B. P. Ronald,[2] and K. W. Anderson[3]

Contribution from the Department of Chemistry, University of Washington, Seattle, Washington 98195. *Received August 15, 1986*

Abstract: A careful determination of the extent of rearrangement during epoxide hydration was carried out in conjunction with nuclear magnetic resonance kinetic studies for both propylene and isobutylene oxides. The complete pH–rate profile was mapped at ionic strength 2.0, and solvent kinetic isotope effects were determined for several limbs. Spectrophotometric analysis of the quantity of aldehyde formed by rearrangement in both the acidic and spontaneous limbs reveals that ionic strength has a profound effect. At ionic strength zero, more rearrangement product is generated in the acidic limb, whereas at ionic strength 2.0, larger amounts of aldehyde are formed in both regions. These results support the conclusion that a different carbocationic intermediate exists in the reaction mechanism for the acidic and spontaneous regions. The experimental observations of the spontaneous region can be explained by the existence of zwitterionic intermediate III. Observed solvent kinetic isotope effects, $k_{H_3O^+}/k_{D_3O^+}$, $k^{H}_{spon}/k^{D}_{spon}$, of 0.33 ± 0.02, 1.78 ± 0.25 and 0.35 ± 0.03, 1.48 ± 0.27 for propylene and isobutylene oxides, respectively, were dissected into components on the basis of classical product studies. At high ionic strength, isolation of compound I, an isobutyraldehyde isobutylene glycol acetal, supports the existence of intermediate III. Apparent partitioning ratios for both the β-hydroxy carbocation, II, and the zwitterion, III, are examined and contrasted. Detailed mechanistic proposals are advanced, and their congruence with a variety of observations described previously in this journal is outlined.

Several channels have been identified from which reaction products may emerge in the ring opening of epoxides.[1b–d,4–13] The pH–log rate profiles associated with the reactions in aqueous media are multiphasic; yet the same vicinal diol product is obtained in each limb, irrespective of which rate law prevails.[11,12] Data pertaining to the nature of the reaction mechanism for the acid-catalyzed limb have been interpreted in terms of a spontaneous opening of the epoxide conjugate acid to generate a β-hydroxy carbocation.[11–14] Subsequent capture by water leads to vicinal diol, while other nucleophilic species produce the corresponding β-substituted alcohols.[7,8] Two isomeric substitution products form concurrently when unsymmetrically substituted epoxides undergo opening (Scheme I). The preferred mode of approach of the nucleophile appears to be from the rear since inversion of configuration is the predominant stereochemical result in the few cases examined.[4,5,15]

Scheme I



Within the pH-independent portion of the profile, where the spontaneous hydrolytic reaction occurs, mechanistic evidence is sparse and remains inconclusive. The "normal" to "abnormal" adduct proportion differs from that found in either the acidic or basic limbs, and it has been documented recently that phosphate buffers catalyze the hydrolytic process in addition to becoming incorporated into products.[1b,c] A more detailed examination of the mechanism operative in this region is desirable, as the conclusions would be fundamental toward understanding the nature of these buffer-catalyzed processes.

A channel that has received scant systematic attention is the one conducive to epoxide rearrangement. This transformation, usually observed under acidic conditions in polar, nonnucleophilic solvent systems, closely resembles the pinacolic rearrangement, a mechanistically well established reaction.[4,5,12,16–21] The present

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(1) We gratefully acknowledge the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation, and the National Institutes of Health of the U.S. Public Health Service for support of this research. (a) Part 7 of a continuing study devoted to the examination of the role of epoxides in vicinal diol dehydrations. (b) Part 6: Pocker, Y.; Ronald, B. P. *J. Phys. Chem.* **1984**, *88*, 4185–91. (c) Part 5: Pocker, Y.; Ronald, B. P.; Ferrin, L. *J. Am. Chem. Soc.* **1980**, *102*, 7725–32. (d) Part 4: Pocker, Y.; Ronald, B. P. *J. Am. Chem. Soc.* **1980**, *102*, 5311–6.

(2) Visiting Scholar from the Department of Chemistry, Idaho State University, Pocatello, ID 83209.

(3) National Science Foundation Undergraduate Research Participant during the period May–August 1978.

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study was designed to address the issue of whether vestiges of this rearrangement process take place in purely aqueous media and to establish the relationship of this channel to those previously mentioned. Is the presence of an acidic reagent critical for the inception of the rearrangement process? How do the different regiochemical results arise? This work probes these questions through carefully executed product and rate studies on propylene and isobutylene oxides in both the acidic and pH-independent regions of the profile at several ionic strengths. Solvent kinetic isotope effect data are combined with isotopic tracer studies in an analysis of the mechanistic routes leading to both vicinal diol and rearrangement products.

Experimental Section

Chemicals. Isobutylene was prepared by the dehydration of *tert*-butyl alcohol with 85% phosphoric acid by using a modification of the procedure for the synthesis of cyclohexene.[22] The gaseous alkene was condensed and stored at −78 °C until required for use.

Isobutylene oxide was prepared by *m*-chloroperoxybenzoic acid oxidation of the alkene in CH_2Cl_2 solution at 5 °C via the procedure described previously.[23,24] Crude product was fractionally distilled several times to give kinetic quality material of boiling range 49.5–51.0 °C. Purified epoxide was stored at −5 °C over anhydrous sodium sulfate and refractionated immediately prior to use. Both isobutylene and isobutylene oxide gave satisfactory proton and ^{13}C NMR spectra. Spectrophotometric analysis of purified epoxide revealed that it contained 0.41 mol % isobutyraldehyde.

Propylene oxide (Aldrich) was purified as previously described.[1b,c] Spectrophotometric analysis of purified material revealed that it contained 0.013 mol % of the propionaldehyde. Tetramethylethylene oxide was prepared as previously described.[1d,24] Sodium dihydrogen phosphate, sodium monohydrogen phosphate, and sodium perchlorate for the preparation of solutions have been described previously.[1b–d]

Propionaldehyde, isobutyraldehyde, and pinacolone for UV spectroscopic and hydration studies were purified by three fractional distillations and stored over anhydrous sodium sulfate at −5 °C until required. Absorbance maxima for the $n \rightarrow \pi^*$ transition were located at 277.5 nm, ϵ 19.3 (water) for propionaldehyde; 280 nm, ϵ 20.9 (water) for isobutyraldehyde; and 278 nm, ϵ 29 (0.2 M perchlorate) for pinacolone.

Measurements. Measurements of proton and ^{13}C NMR spectra, UV-vis spectra, and pH have been described previously.[1b–d,24] NMR kinetic measurements were performed as previously described.[1c,24]

Product Analysis. The extent of rearrangement of both propylene and isobutylene oxides taking place during hydrolysis was computed by determining the quantity of free aldehyde and adding to it the amount of aldehyde hydrate present at equilibrium. Tetramethylethylene oxide rearrangement was measured directly. Measurements were made on a Varian Model 219 UV-vis recording spectrometer connected to a Forma-Temp Jr. Model 2095 water bath and circulator to maintain temperature control over both reference and sample cell compartments. Temperature control was maintained to within ±0.1 °C of the desired setting and was checked periodically by measuring the temperature of the contents of the cuvettes. The concentration quotient for the aldehyde–aldehyde hydrate equilibrium reaction was computed from data derived from observing the aldehyde hydration process in the same medium and at the same wavelength and temperature as obtained in the product studies. The absorbance during the hydration reaction was followed between 3 and 4 half-life times (half-life times ranged from 20 to 80 s) and again after 10 half-life times; resulting log $(A_t - A_\infty)$ versus time plots were linear for up to 75–87% of the hydration reaction. The initial absorbance A_i was determined both by extrapolation to zero time graphically and by using a semilog least-squares program.[1c] Values of A_i and A_∞ were used to compute the hydration equilibria concentration quotient.[25]

Spectrophotometric measurements were performed upon the pure epoxide substrates in water solution at ionic strength 0.0 and a pH (7.6) where there would be no appreciable reaction during the period of observation. Thus, the minute but detectable amount of aldehyde contaminating each epoxide was determined.

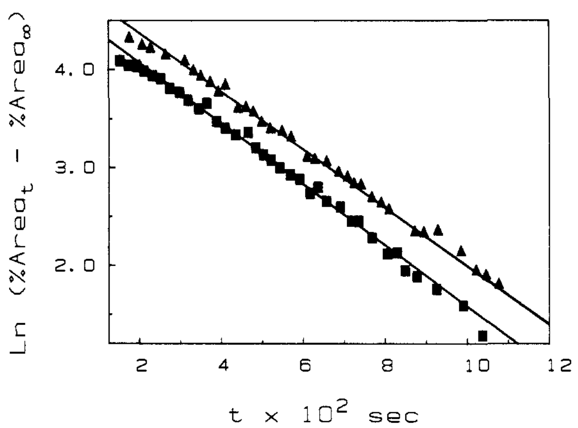

Figure 1. Repetitive integration data from the hydrolysis of isobutylene oxide at 35 °C and ionic strength 2 plotted as log (% Area$_t$ − % Area$_\infty$) versus time. Least-squares treatment of this data yielded the rate coefficients and intercepts, which are respectively (2.72 ± 0.05) × 10^{-3} s^{-1}, 126.45 ± 2.65 (upper line) and (2.86 ± 0.06) × 10^{-3} s^{-1}, 122.45 ± 2.29 (lower line). The lower line was displaced by 20% for clarity.

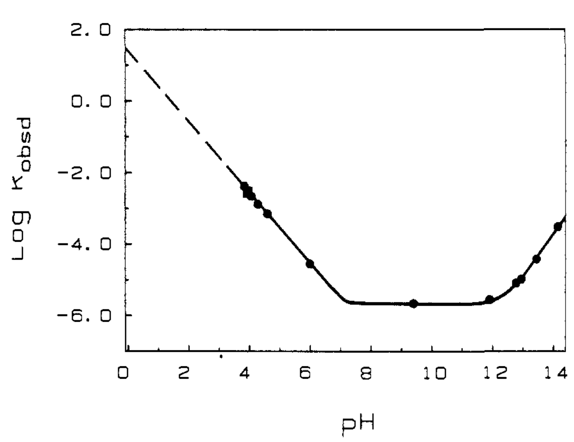

Figure 2. A plot of log k_{obsd} versus pH for the hydration reaction of isobutylene oxide at ionic strength 2.0 and 35 °C. The average of the rate coefficients from Figure 1 is plotted as (■). Three limbs are discernible, the descending limb from pH 3.5 to 6, a horizontal or pH-independent limb from pH 8 to 11, and an ascending limb from pH 12 to 14. The slope of the descending limb is −0.997 ± 0.013 with an intercept that yields a specific hydronium ion rate coefficient, $k_{H_3O^+}$ = 25.8 ± 1.7 M^{-1} s^{-1} with correlation coefficient 0.9998. The spontaneous rate coefficient, k_{spon}, in the pH-independent limb was measured as (2.19 ± 0.57) × 10^{-6} s^{-1}. This value was satisfactorily confirmed by using the points along the curved portion of the ascending limb (pH 11–13) to solve a set of simultaneous equations yielding k^{calcd}_{spon} = (2.13 ± 0.18) × 10^{-6} s^{-1}. The slope of the ascending limb is 1.18 ± 0.07 with an intercept yielding a specific hydroxide rate coefficient, k_{OH^-} = (1.95 ± 0.03) × 10^{-4} M^{-1} s^{-1} and a correlation coefficient of 0.9979.

Duplicate solutions of the epoxide at the same concentration, pH, and ionic strength as obtained in the NMR kinetic studies were allowed to react to completion. These solutions were then analyzed for carbonyl compound both by recording the UV-vis absorption spectrum and by observing the absorbance at the wavelength employed in the hydration studies. Absorbance data were recorded three to four times for each sample. The temperature employed in the aldehyde hydration studies was maintained during the course of an analysis.

Mass spectra were obtained on a Hewlett-Packard Model 5985A GC-MS system fitted with a 30-m J&W DB-5 fused silica capillary column. Analytical data found for isobutyraldehyde isobutylene glycol acetal (2-isopropyl-4,4-dimethyl-1,3-dioxolane) were as follows: $[M]^{\cdot+}$ (*m/z* 144), $[M-1]^+$ (*m/z* 143), and base peak $[M-43]^+$ (*m/z* 101). ^{13}C NMR chemical shifts (internal TMS) and multiplicities were as follows: 106.9 (d), 75.6 (t), 31.6 (d), 25.9 (q), 24.3 (q), 16.1 (q) and 15.8 (q). The quaternary carbon resonance was not detected. Proton chemical shifts (internal TMS), multiplicities, number of hydrogens by integration and coupling constant were as follows: 0.97 (d, 6 H, *J* = 6.4 Hz), 1.33 (s, 6 H), 1.4–2.0 (m, 1 H), 3.36 (s, 2 H), and 4.78 (d, 1 H, *J* = 4.5 Hz).

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Table I. Summary of Rate Coefficients and Isotope Effects for Various Epoxides at Ionic Strength 2.0[a] and 35 °C[b]

oxide[c]	k^{H}_{spon}, s^{-1}	k^{D}_{spon}, s^{-1}	$k_{H_3O^+}$, M^{-1} s^{-1}	$k_{D_3O^+}$, M^{-1} s^{-1}	k_{OH^-}, M^{-1} s^{-1}	$k^{H}_{spon}/k^{D}_{spon}$	$k_{H_3O^+}/k_{D_3O^+}$
propylene	(1.13 ± 0.06) × 10^{-6}	(6.30 ± 0.54) × 10^{-7}	(0.14 ± 0.01)	(0.42 ± 0.04)	(2.99 ± 0.12) × 10^{-4}	(1.79 ± 0.25)	(0.33 ± 0.02)
isobutylene	(2.16 ± 0.18) × 10^{-6}	(1.46 ± 0.14) × 10^{-6}	(2.58 ± 0.17) × 10^{1}	(7.35 ± 0.19) × 10^{1}	(1.95 ± 0.03) × 10^{-4}	(1.48 ± 0.27)	(0.35 ± 0.03)
tetramethyl-ethylene	(2.80 ± 0.27) × 10^{-7}	(1.57 ± 0.10) × 10^{-7}	(3.9 ± 0.19) × 10^{1}	(1.12 ± 0.03) × 10^{2}		(1.78 ± 0.29)	(0.35 ± 0.04)

[a] Sodium perchlorate was used to control ionic strength. [b] The temperature was controlled by the probe of the NMR. [c] The molarity of the epoxides ranged from 0.7 to 0.9 M (propylene oxide), 0.5–0.7 M (isobutylene oxide) and 0.2–0.3 M (tetramethylethylene oxide). All values accompanied by SD.

Results

Isobutylene oxide hydration was conveniently followed by proton NMR spectroscopy. Kinetic measurements were made by observing the epoxide methyl resonance. Between 30 and 120 integrals (depending upon the reaction velocity) were recorded as a function of time during the course of a kinetic run. Typical data for epoxide disappearance followed for 3-5 half-life times of the reaction and plotted as log [%(Area$_t$) − %(Area$_\infty$)] versus time are shown in Figure 1. Duplicate runs were made at ionic strength 2.0 and 35.0 °C over the pH range from 3.5 to 14, generating the pH–rate profile shown in Figure 2. A different rate expression pertains to each limb. The average of the illustrated rates in Figure 1 appears as the enlarged point in Figure 2.

Least-squares treatment of kinetic data for the acidic limb generated a slope of −0.997 ± 0.013 with an extrapolated intercept that gave $k_{H_3O^+}$ = 25.8 ± 1.7 M^{-1} s^{-1}. A $k_{D_3O^+}$ = 73.5 ± 1.9 M^{-1} s^{-1} was obtained analogously from measurements made in fully deuteriated media. The experimental solvent kinetic isotope effect, 0.35 ± 0.03, was found to compare favorably with that previously determined for the hydration reaction of both propylene and tetramethylethylene oxides under similar conditions (Table I). Isobutylene oxide to the extent of 2.40 ± 0.06% was converted into isobutyraldehyde by rearrangement (Table II). The remaining 97.60 ± 0.06% was hydrated to form glycol.

In the horizontal portion of the pH–rate profile a slow spontaneous hydration reaction takes place. The value of the rate coefficient was measured as k^{H}_{spon} = (2.19 ± 0.57) × 10^{-6} s^{-1} in the pH region between 9 and 10, where neither acid nor base make a catalytic contribution. The accuracy was confirmed by solving the set of simultaneous equations with rate data measured in the pH region between 12 and 13 where both spontaneous and base-catalyzed processes contribute to the total rate expression (computed value k^{H}_{spon} = (2.13 ± 0.18) × 10^{-6} s^{-1}). In fully deuteriated media the spontaneous reaction has a k^{D}_{spon} = (1.46 ± 0.14) × 10^{-6} s^{-1}. The solvent kinetic isotope effect, $k^{H}_{spon}/k^{D}_{spon}$ of 1.48 ± 0.27, compares favorably with data for other epoxides (Table I). Aldehyde to the extent of 2.50 ± 0.02% generated from rearrangement was observed in this pH region, while the balance of the epoxide was converted into glycol. The pH–rate profile was extended into the base-catalyzed region to verify the rate coefficient for the spontaneous reaction.

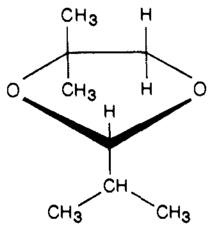
The rearrangement channel is active during the hydration reaction leading to the formation of small but definite amounts of propionaldehyde and isobutyraldehyde from their respective epoxides. An instructive comparison can be made by examining the results at ionic strength 0.0 and 2.0 (Table II). Apparently, more rearrangement occurs within the spontaneous region at ionic strength 2.0 than in the acidic region; clearly, the opposite is true at ionic strength 0.0. A comparison of isobutylene and tetramethylethylene oxides shows that although both substances possess tertiary reaction centers, more rearrangement occurs at ionic strength 2.0 for the former than the latter.

Table II. Percentage Hydration and Rearrangement for Several Epoxides under Various Conditions

oxide	ionic strength	pH	mol %[a]	
			hydration[b]	rearrangement[c]
propylene	0.0[d]	7.6	99.99 ± 0.005	0.01 ± 0.005
	0.0[d]	3.5	99.97 ± 0.005	0.03 ± 0.005
	2.0	8.6	99.74 ± 0.03	0.26 ± 0.03
	2.0	3.9	99.78 ± 0.04	0.22 ± 0.04
isobutylene	0.0[d]	7.6	99.80 ± 0.01	0.20 ± 0.01
	0.0[d]	4.6	99.26 ± 0.07	0.74 ± 0.07
	2.0	8.6	97.50 ± 0.02	2.50 ± 0.02
	2.0	3.9	97.60 ± 0.06	2.40 ± 0.06
	4.1[e]	8.4	95 ± 1	5 ± 1
tetramethyl-ethylene[f]	0.0[d]	2.6	99.92 ± 0.005	0.08 ± 0.005
	2.0	2.3	99.86 ± 0.05	0.14 ± 0.05
	4.0	2.0	99.76 ± 0.10	0.24 ± 0.10
	6.0	1.6	97.40 ± 0.40	2.60 ± 0.40

[a] Derived from the amount of aldehyde as measured by UV absorption spectrometry and the initial amount of epoxide added to the reaction mixture. The temperature was controlled at 25.0 ± 1.0 °C for the period of 2 months during the course of these reactions. The ionic strength was maintained at 2.0 with sodium perchlorate. Values are accompanied by standard deviations. [b] Calculated by subtracting the amount of rearrangement from 100%. [c] Corrected for the trace amount of carbonyl compound present in the epoxide substrate by observing the absorbance at the λ_{max} of the carbonyl compound under conditions of pH where no reaction could take place during the course of the measurement. This standard error was determined from runs made in duplicate with quadruplicate readings of the absorbance for each run. [d] The ionic strength of these solutions was below 10^{-2}. [e] In addition to isobutylene glycol, a dimeric product having the structure I was isolated to the extent of 10.1%. Since exactly half of this structure has a rearranged skeleton only half of the total amount of dimer was reported as rearrangement product. [f] Data derived from both UV spectrometric and NMR measurements of the amount of ketone formed at 25.0 ± 1.0 °C. More precise control of temperature was not possible over the long period required for this reaction to go to completion.

At even higher ionic strength (4 M sodium perchlorate) in the spontaneous rate region (pH ~8) the behavior of these epoxides contrasts with that of tetramethylethylene oxide, Propylene oxide only reacted partially after two months while isobutylene oxide, though not completely soluble, produced an oil whose volume increased over the period of reaction. After 60 days an NMR spectrum of the aqueous portion indicated that the reaction was essentially complete. A sample of the oil was withdrawn and examined by both ^1H and ^{13}C NMR and by GC-MS. The simplicity of these spectra coupled with a molecular ion of mass 144, and a base peak at mass 101 ([M − 43]$^+$, loss of an isopropyl group) support the conclusion that this oil has the structure of an isobutylene oxide dimer, I. Compound I is an acetal composed of isobutylene glycol and isobutyraldehyde. Under the neutral conditions of its formation, the acetal as well as isobutylene glycol was stable toward further reaction. The amount formed under these conditions was 10.1% indicating that a minimum of 5% rearrangement must have taken place.



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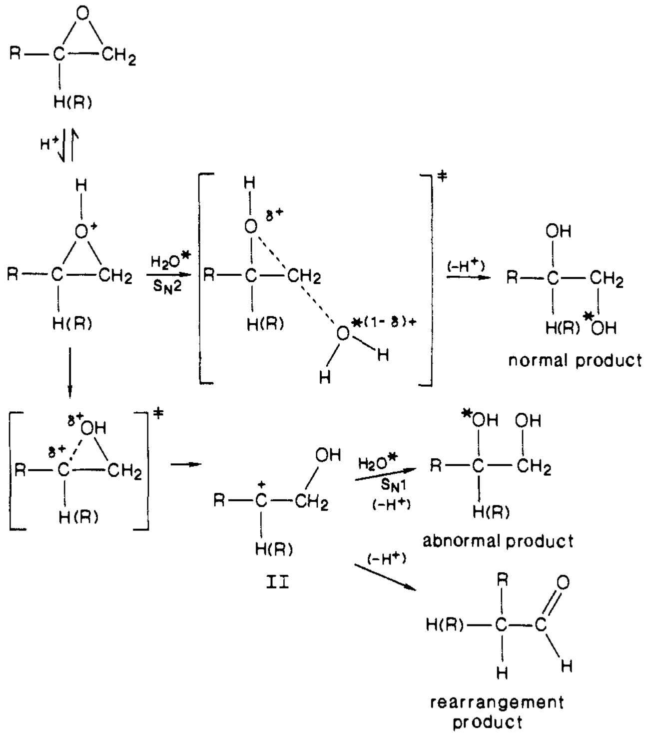
Regiochemistry of the addition process for propylene and isobutylene oxides was also examined. Table III compares data with those derived from other workers. Significant amounts of addition

Table III. Regiochemistry of Ring Opening of Propylene Oxide (**1**) and Isobutylene Oxide (**2**) with Various Nucleophiles in Aqueous Solution[a]

reactive form of epoxide	epoxide[b]	pH	nucleophile	% normal adduct[c]	% abnormal adduct[d]	reference
H-bonded	**1**	7.0	H_2O	64 ± 3	36 ± 3	11b, 13a
		7.0	HPO_4^{2-}	48 ± 2	52 ± 2	1c, this work
		7.0	Cl^-	88 ± 1	12 ± 1[e]	7, 8
	2	7.0	H_2O	(9–20) ± 3	(91–80)[f] ± 3	11b, 13a
protonated	**1**	1.0	H_2O	30 ± 3	70 ± 3	11b, 13a
		3.8	Cl^-	66 ± 1	34 ± 1[g]	7, 8
		4.0	HCO_2^-	50 ± 5	50 ± 5[g]	1c, this work
	2	1.0	H_2O	1 ± 3	99 ± 3	11b, 13a

[a] All product ratios listed herein were those determined under kinetic control. Reaction products were independently shown to be stable during the course of the experiments except where noted. Values are accompanied by standard deviations. [b] A complete kinetic analysis including solvent isotope effects studies allowed the nucleophile to be determined and the reactive form of the epoxide to be identified. A complete pH–rate profile was determined in H_2O media. [c] The normal adduct is defined as the product derived from attack by the nucleophile at the least hindered position of the epoxide (see Scheme I). [d] The abnormal adduct is defined as the product derived from attack of the nucleophile at the most hindered position of the epoxide (see Scheme I). [e] The error in these determinations was less than 2%. [f] The authors in ref 11b and 13a indicate that the acid-catalyzed reaction was not completely suppressed, thus leading to a high proportion of abnormal adduct in their observed product ratio. [g] In formate buffers propylene oxide forms two adducts; however, these monoformate esters are kinetically unstable under the experimental conditions and only estimates of their relative abundance could be made. See ref 1c.

Scheme II[a] Mechanism in the Acidic Limb



[a] An asterisk traces the fate of a reacting water molecule (R = CH_3).

product arise when phosphate buffers are employed.

Discussion

Although the rearrangement of epoxides represents a minor product channel, its very existence is a factor that must be considered in the mechanism of ring opening. In aqueous media, the carbocationic intermediate, in addition to giving rearranged material, forms adduct through the capture of water. Comparison of the extent of rearrangement relative to adduct formation in both the acidic and spontaneous limbs of the pH–rate profile provides useful diagnostic information with regard to mechanism.

Within the acidic region, Long and co-workers showed through elegant isotopic tracer studies that the glycol product formed during hydrolysis arose by two modes.[11b] Because the normal mode of reaction took place at the least sterically hindered center, the S_N2 pathway was invoked in its description. Reaction at the more highly substituted ring carbon (abnormal adduct) was ascribed to an S_N1 mechanism. Noteworthy is the observation that abnormal adduct constitutes a major proportion of the product in this limb (Table III). The concurrent rearrangement pathway, whose extent is measured and documented in Table II, had not been established experimentally at that time.

The solvent kinetic isotope effects are consistent with the mechanistic conclusions made about this region of the profile (Table I). These values, composed of equilibrium and secondary isotope effects, support the conclusion that the epoxide oxygen is protonated in a fast equilibrium step followed by rate-determining C–O bond fission. Additional insight can be gained by separation of these data into their logical mechanistic components. This dissection uses Long and co-workers' product analysis coupled with Schowen's values for the isotope effect expected from each path.[11b,26] In this analysis if the S_N1 component is accorded a carbocationic-like transition state and the S_N2 component assigned a reactant-like transition state, observed isotope effects for both propylene oxide and isobutylene oxide can be reproduced with a high degree of accuracy.[26,27] Corroborative results from a similar dissection of the volume and entropy of activation would be desirable, but the diagnostic utility of these parameters has yet to achieve the level of refinement reached with solvent isotope ef-

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(26) Schowen, R. L. *Prog. Phys. Org. Chem.* **1972**, *9*, 275–332.

(27) Dissection of Acidic Limb Solvent Isotope Effects

		S_N1 process isotope effect	
		transition state	
epoxide	% abnormal product	substrate like	product like
ethylene			
propylene	70	0.43–0.29	
isobutylene	99	0.43–0.29	

		S_N2 process isotope effect		
		transition state		
epoxide	% normal product	substrate like	product like	observed isotope effect
ethylene	100	0.43–0.67		0.45 ± 0.07
propylene	30	0.43–0.67		0.33 ± 0.02
isobutylene	1	0.43–0.67		0.35 ± 0.03

The total isotope effect for the hydrolysis reaction was computed by using the equation below with individual isotope effect components from ref 26.

(% abnormal product × isotope effect)/100 +
(% normal product × isotope effect)/100 = total solvent isotope effect

Ethylene oxide (S_N2 substrate like transition state): (100 × 0.43)/100 = 0.43.

Propylene oxide (S_N1 product like transition state + S_N2 substrate like transition state): (70 × 0.29)/100 + (30 × 0.43)/100 = 0.33.

Isobutylene oxide (S_N1 product like transition state + S_N2 substrate like transition state): (99 × 0.29)/100 + (1 × 0.43)/100 = 0.29.

Table IV. Apparent Partitioning Ratios, *r*, for Various Epoxides in Aqueous Media Assuming Both Products Originate from a Carbocationic Intermediate at 25 °C[a]

epoxide	ionic strength	pH	partitioning ratio, $r^{b,c}$	% $\Delta r/r$
propylene oxide	2.0	3.9[d]	$(3.2 \pm 0.8) \times 10^2$	$(1.3 \pm 0.7) \times 10^2$
	2.0	8.6	$(1.4 \pm 0.4) \times 10^2$	
	0.0	3.5[d]	$(2.3 \pm 0.6) \times 10^3$	$(3.6 \pm 3.4) \times 10^1$
	0.0	7.6	$(3.6 \pm 2.5) \times 10^3$	
isobutylene oxide	2.0	3.9[d]	$(4.0 \pm 0.3) \times 10^1$	$[(2.9 \pm 0.4)-(1.1 \pm 0.1)] \times 10^1$
	2.0	8.6	$[(3.1 \pm 0.2)-(3.6 \pm 0.2)] \times 10^1$	
	0.0	4.6[d]	$(1.3 \pm 0.2) \times 10^2$	$-[(7.1 \pm 1.2)-(6.8 \pm 1.2)] \times 10^1$
	0.0	7.6	$[(4.5 \pm 0.5)-(4.0 \pm 0.5)] \times 10^2$	

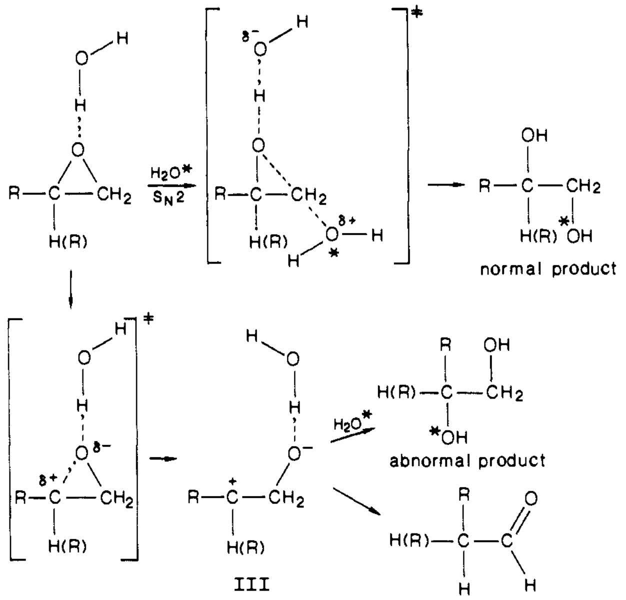
[a] Based upon the data in Tables II and III. The amount of abnormal adduct reported in Table III was corrected for the amount of rearrangement observed in Table II prior to computing the partitioning ratios. Standard deviations accompany entries. [b] The apparent partitioning ratio, *r*, is defined as (abnormal adduct)/(rearrangement product). [c] Values of *r* were calculated in the following manner. The percentage of normal and abnormal adduct as reported in Table III by ref 11b and 13a was corrected for the amount of rearrangement reported in Table II. The corrected value of the percentage abnormal adduct was divided by the percentage of rearrangement to give *r*. Data in the last line of Table III serves as an example, 1% normal adduct, 99% abnormal adduct (Long's data without rearrangement). From Table II (line 6) find the percentage rearrangement, 0.74%. Corrected percentage of abnormal product = 99(100)/(100 + 0.74). (Corrected percentage abnormal product)/percentage rearrangement = *r*. 99(100)/0.74(100 + 0.74) = 1.3 × 10^2, reported in Table IV, line 7. [d] These percentages for abnormal and normal adducts were determined at pH 1, ref 11b and 13a.

fects.[26] Mechanistic deductions for the acidic limb are summarized in Scheme II.

Propylene, isobutylene, and tetramethylethylene oxides undergo spontaneous hydrolysis in the absence of buffers forming the respective glycols as principal products. These reactions are quite slow with pseudo-first-order rate coefficients on the order of 10^{-6}–10^{-7} s^{-1} in the pH region between 7.6 and 8.6 at ionic strength 2. The corresponding second-order rate coefficients of 10^{-8}–10^{-9} M^{-1} s^{-1} calculated from the known concentration of water agree closely with previous data.[13] Substantial amounts of sodium perchlorate, a salt with extremely weak nucleophilic character, reduced the rate of spontaneous hydrolysis.[28] The second to third power dependence upon water concentration found in epoxide hydrolysis delineates the substantive role played in the transition state by selected molecules in the solvation shell.[29]

In the absence of added salt, the amount of rearrangement taking place concurrently with hydrolysis for propylene oxide at pH 7.6 is exceedingly small; though larger with isobutylene oxide, it still constitutes a very small fraction of the total product mixture. A carbocationic intermediate necessarily must exist in this reaction channel in order to account for the presence of rearranged product. This intermediate is also expected to be the major source of abnormal product through capture by water. Of special interest is the observation that, for each epoxide, less rearrangement product is formed in this pH region than in the acidic limb. Indeed a simple change of pH from 3.5 or 4.6 to 7.6 leads to a threefold reduction in the amount of aldehyde formed. In the acidic limb, carbocation II was established as the intermediate (Scheme II). If this same intermediate is invoked to account for the formation of aldehyde in the spontaneous region, then it is necessary to explain why the extent of rearrangement should depend upon pH. There appears to be no direct connection between the partitioning of the carbocation II and the presence of a low concentration of protons in the medium. The hydronium ion concentration in this study (10^{-4} M) is so small compared with other substances that it alters neither the nucleophilicity nor the effective concentration of water and thus can have no measureable effect upon the partitioning of II.

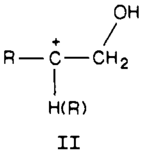
Scheme III[a] Mechanism for the Spontaneous Region



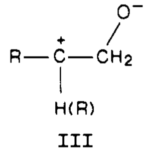
[a] An asterisk traces the fate of a reacting water molecule (R = CH_3).

Adjustment of the ionic strength of the medium to 2 with sodium perchlorate causes the amount of rearranged product to increase by a factor of approximately 25 for propylene oxide; a lesser increase is observed for isobutylene oxide. This salt appears to promote the rearrangement reaction to a greater extent in the spontaneous region than in the acidic limb. If II is invoked as the intermediate here, then why in the presence of so much salt should a low concentration of hydronium ions exert such an effect upon partitioning? The apparent partitioning ratios (Table IV) were obtained by combining data from Long and co-workers with those of the present study.[13a,b]

It is apparent that carbocationic intermediate II cannot satisfactorily explain the results in the spontaneous region. Therefore, another carbocationic intermediate, different from II, must be invoked to account for the rearranged product, the formation of I, and the variation of the apparent partitioning ratio. Zwitterion III differs in structure from II but possesses characteristics that make it appealing as an intermediate for this pH region. Intermediate III would possess an enhanced tendency to undergo both ring closure and to rearrange compared to II.[30] Its negatively charged oxygen atom would facilitate the 1,2-shift of a potential migrating group to the carbocationic center. Capture of water or other nucleophiles by this center would result in the formation of abnormal product. The apparent partitioning ratio for these processes would be expected to display some sensitivity to the structural difference between intermediates II and III. The data presented in Tables II and IV are entirely consistent with the



II



III

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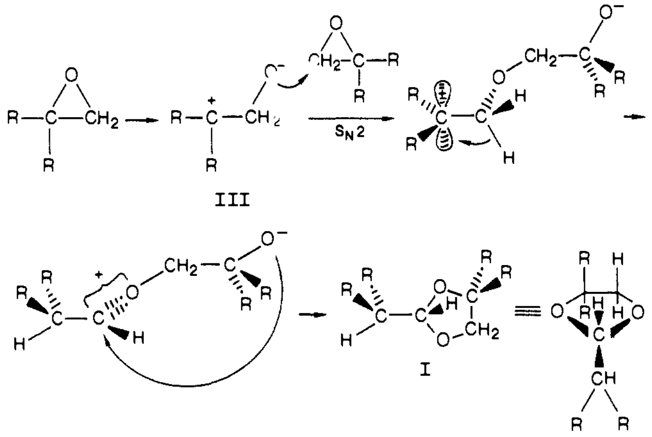
(28) At 35 °C sodium perchlorate depresses the spontaneous rate coefficient from (2.69 ± 0.17) × 10^{-6} at ionic strength 2 to (4.56 ± 0.26) × 10^{-7} at ionic strength 4.

(29) Virtanen, I.; Olavi, P. *Suom. Kemistil. B* **1965**, *B38*, 135–42. Virtanen, I.; Olavi, P. *Soum. Kemistil. B* **1966**, *B39*, 115–22.

(30) Stabilization of III may take place in the presence of electrolytes through the interaction of solvent separated ion pairs with the zwitterion and thus reduce the rate of ring closure. Ukachukwa, V. C.; Blumenstein, J. J.; Whalen, D. L. *J. Am. Chem. Soc.* **1986**, *108*, 5039–40.

Scheme IV. Pathway for Formation of Compound I (R = CH_3)



presence of intermediate III in the spontaneous region while II occurs in the acidic limb.

Intermediate III and the assumption that ring opening is rate limiting are consistent with the results from dissection of the solvent isotope effect into its logical mechanistic components. A value of 1.0–1.3, typical for an S_N1 type reaction, would arise from carbocationic intermediate III.[31] Since abnormal adduct is a minor product in the reaction of propylene oxide, the isotope effect corresponding to this component makes a small contribution to the total. On the other hand, the major portion of the isotope effect issues from the path leading to normal product. This entails an S_N2 type reaction between water and the H-bonded epoxide, with the possible participation of a third molecule of water.[29,31,32] A typical S_N2 reaction for alkyl halides has a solvent kinetic isotope effect of about 1.3; however, for epoxides, additional proton transfer processes involving water may raise the value to 1.8 or higher.[26] The same analysis applies to isobutylene oxide except that the relative proportions from each pathway differ. The isotope effect from the normal product path is small, while the major portion arises from the route involving intermediate III. These simple calculations reproduce the observed solvent isotope effect in a manner that reflects favorably upon the mechanistic model described herein.

Scheme III summarizes the conclusions from this work. A bimolecular reaction between water and the H-bonded epoxide leads to normal product. Both abnormal and rearranged product arise from intermediate III.[33] The delicate balance between these two paths determines the magnitude of the solvent isotope effect and the sensitivity of the reaction rate to ionic strength. Table III shows the proportions of abnormal and normal adduct that arises when different nucleophilic species are present in the medium. These proportions reflect the competition between attack upon the H-bonded epoxide and spontaneous formation of intermediate III. Substance I, formed during the hydrolysis of isobutylene oxide at ionic strength 4 is consistent with intermediate III (Scheme IV).[33]

Conclusion

The similarities and differences between intermediates II and III account for previous difficulties encountered in the mechanistic characterization of the spontaneous as opposed to the acidic region. The distinction between the two becomes apparent when a direct comparison is made of the extent of rearrangement as a function of ionic strength in these two pH regions. The dissimilar values for the solvent kinetic isotope effects at pH 4 and 8 signal that mechanistic changes have taken place but fail to reveal their precise nature. Schemes II and III are proposed for the mechanism of reaction in the acidic and spontaneous regimes, respectively, and account for the experimental observation of rearrangement. Analysis of the solvent isotope effect data provides support for these proposals. Isolation of a dimeric product from the reaction of isobutylene oxide at high ionic strength is evidence for the transient existence of intermediate III.

Acknowledgment. K.W.A. gratefully acknowledges the NSF for an Undergraduate Research Participant Award. We thank Dr. George E. Renzoni, Research Scientist II Analytical and Spectral Services (1982–86), Department of Chemistry, University of Washington, for performing ^{13}C NMR and GC–MS measurements on compound I.

Registry No. D_2, 7782-39-0; isobutylene oxide, 558-30-5; propylene oxide, 75-56-9.

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[31] Dissection of Spontaneous Region Solvent Isotope Effects

epoxide	% abnormal product	S_N1 process isotope effect, transition state: substrate like	product like
ethylene			
propylene	36	1.0–1.3	
isobutylene	91–80	1.0–1.3	

epoxide	% normal product	S_N2 process isotope effect, transition state: substrate like	product like	observed isotope effect
ethylene	100	1.0–2.0		
propylene	64	1.0–2.0		1.79 ± 0.3
isobutylene	9–20	1.0–2.0		1.48 ± 0.3

The total isotope effect for the hydrolysis reaction was calculated by using the equation below. See ref 32.

(% abnormal product × isotope effect)/100 +
(% normal product × isotope effect)/100 = total solvent isotope effect

Ethylene oxide (S_N2 product like transition state): (100 × 2.0)/100 = 2.0.

Propylene oxide (S_N1 product like transition state + S_N2 product like transition state): (36 × 1.3)/100 + (64 × 2.0)/100 = 1.7.

Isobutylene oxide (S_N1 product like transition state + S_N2 product like transition state): (91 × 1.3)/100 + (9 × 2.0)/100 = 1.4 or (80 × 1.3)/100 + (20 × 2.0)/100 = 1.4.

[32] The S_N2 product like transition state in ref 31 contains two water molecules, one acting as a nucleophile and the other assisting through H-bond formation. Although additional water molecules could be involved in the reaction and lead to a larger isotope effect, between two and three water molecules have been implicated on the basis of the dependency of rate on the water concentration (ref 29). The S_N1 product like transition state is strongly zwitterionic. A major factor contributing to the isotope effect for zwitterion formation is a change in solvation. This magnitude is estimated to be similar to that found in solvolysis reactions (ref 26).

[33] Capture of a water molecule at the carbocationic site of zwitterion III leads to abnormal product while hydride migration from the primary carbon to the carbocationic center generates aldehyde. An alternative mode of aldehyde formation suggested by the referees involves proton removal from III, generating an enolate. In our view, conversion of III into aldehyde closely resembles the pinacolic rearrangement whose intramolecular nature predisposed us to depict the hydride migration path.