

Activation Parameters and Mechanism of the Acid-catalysed Hydrolysis of Epoxides

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Rates of acid-catalysed hydrolysis of three epoxides have been measured over the temperature range 0–30°. The energies of activation are within the range 18–21 kcal mol⁻¹. The entropies of activation are -8 for epichlorohydrin, -5 for propylene oxide, and +8 cal mol⁻¹ K⁻¹ for isobutylene oxide. The significance of these values and related factors are discussed in relation to the A-2 mechanism in the case of epichlorohydrin and propylene oxide and the A-1 mechanism in the case of isobutylene oxide.

THE review literature on epoxides gives many examples of nucleophilic ring-opening reactions in aqueous solution [equation (1)].¹⁻⁷ In equation (1), X⁻ is a nucleophilic anion. When the nucleophile is the neutral water molecule, the forward reaction occurs as in

equation (2), but there is no detectable reverse reaction in aqueous solution.⁸ Owing to the relatively low nucleophilic activity of water, this is generally one of the slowest reactions of epoxides.

Reaction (2) is greatly accelerated by hydrogen ions,

¹ S. Winstein and R. B. Henderson, in 'Heterocyclic Compounds,' ed. R. C. Elderfield, Wiley, London, 1950, vol. 1, ch. 1.

² E. L. Eliel, in 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, London, 1956, ch. 2.

³ R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.

⁴ F. H. Newth, *Quart. Rev.*, 1959, **13**, 30.

⁵ A. D. Cross, *Quart. Rev.*, 1960, **14**, 317.

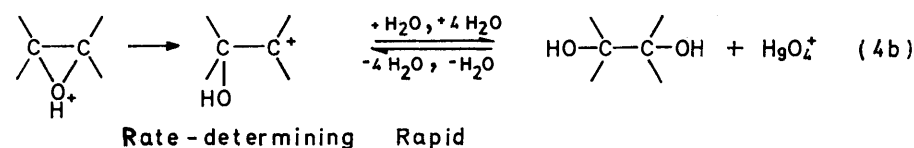
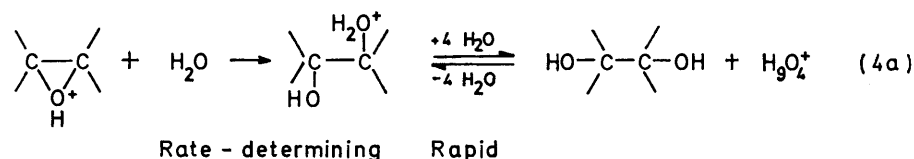
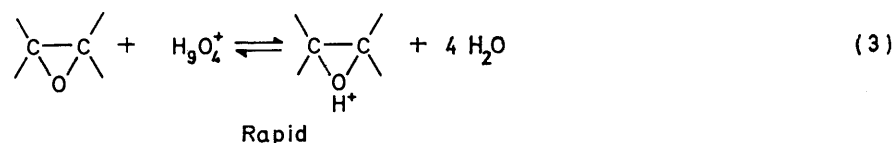
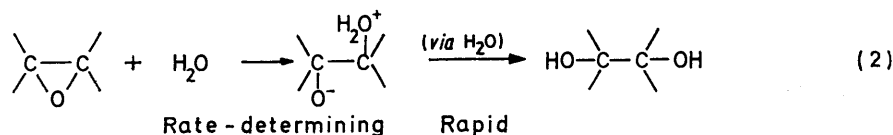
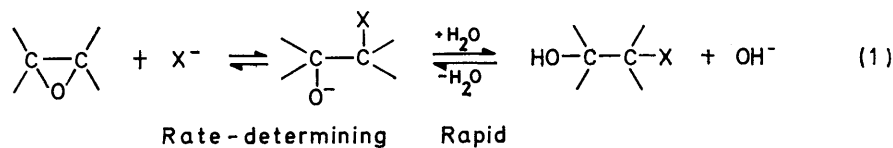
⁶ A. Rosowski, in 'Heterocyclic Compounds with Three and Four Membered Rings, Part I,' ed. A. Weissberger, Interscience, London, 1963, ch. 1.

⁷ Y. Ishii and S. Sakai, in 'Ring-opening Polymerisation,' ed. K. C. Frisch, Dekker, New York, 1969, vol. 2, ch. 1.

⁸ J. G. Pritchard and F. A. Long, *J. Amer. Chem. Soc.*, 1956, **78**, 6008.

particularly in the case of epoxides which have electron-releasing substituents on the ring carbon atoms.⁹ Regarding the mechanism of the acid-catalysed hydrolysis, there is first a preliminary equilibrium, characteristic of specific acid catalysis, in which a relatively very small

undoubted nucleophilic reaction (4a). As a basis for further discussion and an attempt at some clarification of the matter, we present the results of a study on energies and entropies of activation for the acid-catalysed hydrolysis of some typical epoxides.



amount of the conjugate acid of the epoxide is formed [equation (3)]. This step is supported by accurately first-order kinetics, direct proportionality of the rate coefficients to the Hammett acidity function, and an appropriate solvent deuterium isotope effect.⁸⁻¹⁰ Regarding the following step, in this paper the nucleophilic participation of water in certain examples of this reaction is in question, the two extremes in the case being illustrated in equations (4a) and (4b). This matter has not been clear for many years, owing to conflicting evidence.¹¹ Step (4a) has been universally anticipated from the existence of the noncatalysed nucleophilic reactions (1) and (2), but the spontaneous ring-opening reaction (4b) was first suggested by Winstein and Henderson¹ and also later by Ingold.¹² For certain epoxides, reaction (4b) may be sufficiently rapid to be more important than the

⁹ J. G. Pritchard and F. A. Long, *J. Amer. Chem. Soc.*, 1956, **78**, 2667.

¹⁰ J. N. Bronsted, M. Kilpatrick, and M. Kilpatrick, *J. Amer. Chem. Soc.*, 1929, **51**, 428.

¹¹ C. A. Bunton, 'Nucleophilic Substitution at a Saturated Carbon Atom,' Elsevier, London, 1963, p. 157.

EXPERIMENTAL

The dilatometric method, the application of tetramethylpyrazine-perchlorate buffer to the study of the kinetics of acid-catalysed hydrolysis of isobutylene oxide at *ca.* 25°, and the precision in pH control and rate measurement attainable have been described.¹³ This study has now been extended from 29 to 4°. Temperatures were checked against a thermometer calibrated to within ±0.05° at the National Physical Laboratory. A Dynacap pH-meter was used to measure pH with respect to standards accurate to ±0.005 at the appropriate temperatures. Experiments were at pH 3.50 ± 0.005 in most cases. The observed first-order rate coefficients were corrected for small variations of initial pH and temperature in certain cases in which one or both of these differed slightly from the values reported.

A similar kinetic technique has been applied to epichlorohydrin and propylene oxide in, respectively, 0.392 and 0.01M-aqueous perchloric acid (without buffer). These acid solutions were titrated, respectively, with standard sodium

¹² C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' G. Bell, London, 1953, 1st edn., ch. VII.

¹³ J. G. Pritchard and I. A. Siddiqui, *J.C.S. Perkin II*, 1972, 1309.

hydroxide and potassium hydrogen phthalate solutions to establish the hydrogen-ion concentration (C_{H^+}) to within $\pm 0.2\%$.

Second-order rate coefficients (k_{H^+}) were calculated from the first-order dilatometric coefficients (k_1) by the usual relationship $k_1 = k_{H^+} \times C_{H^+}$. First-order rate coefficients for the noncatalysed hydrolysis of the three oxides, for example at 25° , are $1 \times 10^{-6} \text{ s}^{-1}$, or slightly less.^{10,13,14} The corrections necessary to the observed overall first-order rates, in order to arrive at the acid-catalysed hydrolysis rates, were 0.3 for epichlorohydrin, 0.2 for propylene oxide, and 0.05% for isobutylene oxide, *i.e.* negligible in most considerations. The correction due to the contraction of water from 29 to 4° is 0.3% in the opposite direction from the previous correction. Limits were calculated from Gosset's *t* for 99% confidence. Sufficient kinetic data were collected to support least-squares straight lines for $\log k_{H^+}$ against $1/T$ with precision suitable for the calculation of significant activation parameters. Deviations of present and previous data from the least-squares lines were examined graphically.

Epichlorohydrin (Hopkin and Williams) was distilled and a cut taken at 115° , n_D^{21} 1.3655. Similarly, a 32° cut of propylene oxide (H and W) was used, n_D^{25} 1.3638. Chromatography of isobutylene oxide (K and K), n_D^{20} 1.3748, showed no impurity. Tetramethylpyrazine was prepared as previously described,¹³ and inorganic reagents were of AnalaR grade.

RESULTS

Isobutylene Oxide.—Table 1 shows mean values of rate coefficients for the acid-catalysed hydrolysis of isobutylene oxide at pH 3.50 for four temperatures. The 99% confidence limits calculated from the sets of values for each

TABLE 1

Rates of acid-catalysed hydrolysis of epoxides

Temp. (°C)	C_{H^+}/mM	No. of expts.	$10^5 k_1/\text{s}^{-1}$ (Mean)	Deviation ^a in $\log k_{H^+}$
<i>Isobutylene oxide</i>				
4.3	0.316	7	17.4	0.00 ^b
15.1	0.316	7	62.0	-0.01 ^b
25.7 ^c	0.316	8	232 ^a	+0.02 ^b
28.7	0.316	8	271	-0.02 ^b
<i>Propylene oxide</i>				
1.7	10	4	3.11	0.00 ^b
11.7	10	2	11.2	+0.02
24.7	10	5	46.5	0.00 ^b
<i>Epichlorohydrin</i>				
1.7	392	2	1.685	-0.06
3.7	392	1	2.45	0.00
5.7	392	2	3.65	+0.05
7.7	392	2	5.18	+0.09
11.7	392	4	5.81	-0.06
14.7	392	2	11.3	+0.05
19.7	392	3	17.0	-0.02
24.7	392	5	31.5	0.00

^a Deviation of $\log k_{H^+}$ from the least-squares straight line calculated for the variation of $\log k_{H^+}$ with $1/T$. ^b Based on the closest value within the outer limits of the data (otherwise the deviation is for the mean $\log k_{H^+}$). ^c Data from ref. 13.

temperature are ± 2.2 for 4.3, $< \pm 1$ for 15.1, ± 3.3 for 25.7,¹³ and $\pm 1.3\%$ for 28.7°. These limits are close to the outside limits of the data. The time range of the dilatometric experiments for *ca.* 95% reaction of isobutylene oxide

¹⁴ F. A. Long and J. G. Pritchard, *J. Amer. Chem. Soc.*, 1956, **78**, 2663.

was 0.5—6 h, depending on temperature. The least-squares straight line through the four mean values is $\log k_{H^+} = 14.942 - 4.22 \times 10^3/T$. Deviations of the outer limits of our data from the line are random and within ± 0.02 in \log (Table 1), and we assume they may be due to deviations in the pH-meter from month to month. Deviations of the previously measured, single values of k_{H^+} from our line are given in Table 2 and show a much greater scatter typical of data obtained without close pH control.

TABLE 2

Literature values for rates of acid-catalysed hydrolysis of epoxides, and deviations of the derived values of $\log k_{H^+}$ from the least-squares lines of this work

Temp. (°C)	C_{H^+}/mM	$10^5 k_1/\text{s}^{-1}$	$10^5 k_{H^+}/1 \text{ mol}^{-1} \text{ s}^{-1}$	Deviation in $\log k_{H^+}$
<i>Isobutylene oxide</i>				
0.0	0.98	30.5 ^a	31,100	+0.01
0.0	1		38,000 ^g	+0.08
25.0	1		490,000 ^g	-0.12
<i>Propylene oxide</i>				
0.0	24		246 ^d	-0.01
1.0	19.7		279 ^g	-0.02
10.0	19.7		846 ^g	-0.02
30.0	19.7		7450 ^g	-0.03
<i>Epichlorohydrin</i>				
0.0	695 ^{a,b}	4.9 ^e	6.91	+0.09
20.0	100		43.4 ^h	-0.05
25.0	63.5		68.2 ⁱ	-0.10
25.0	97		77 ^j	-0.04
30.0	715 ^{a,c}	141 ^f	129	-0.08

^a For $C_{H^+} > 0.5\text{M}$, $k_{H^+} = k_1/h_0$, where $-\log h_0 = H_0 = -\log a_{H^+}f_B/f_{BH^+}$ (ref. 26). ^b $H_0 = 0$ for perchloric acid. ^c $H_0 = -0.04$ for sulphuric acid. ^d From ref. 16. ^e From ref. 9. ^f From H. Kwart and A. L. Goodman, *J. Amer. Chem. Soc.*, 1960, **82**, 1947. ^g From ref. 15. ^h From ref. 10. ⁱ From ref. 22. ^j From ref. 8.

Propylene Oxide.—Table 1 shows mean values of k_1 for which the outside limits have the range ± 3 —5% (or ± 0.01 —0.02 for $\log k_{H^+}$). The longer time range for the dilatometric measurements (4—50 h) may have contributed to the lower precision here. The least-squares straight line derived from our mean values is $\log k_{H^+} = 12.616 - 4.15 \times 10^3/T$, with which previous values agree reasonably (Table 2).

Epichlorohydrin.—The scatter of primary results for any one temperature was unusually high for this compound (mean scatter *ca.* 20%). The range of times required for the dilatometric experiments was again 4—50 h, and we have no explanation for the poor precision of our measurements in this case. However, the least-squares line calculated from a plentiful number of mean values is $\log k_{H^+} = 11.482 - 4.34 \times 10^3/T$. The average deviation, irrespective of sign, of the mean values from this line is *ca.* 0.04 log units, or 9—10% in k_{H^+} . The deviations are randomly +ve and -ve and we assume our line to be correct within ± 0.04 log units. The deviations of previous measurements from our line show a generally greater scatter (Table 2).

Arrhenius Parameters.—These are shown in Table 3. We confirm the previous value of the entropy of activation for propylene oxide.^{15,16} Our new value for isobutylene oxide is *ca.* 12 units more positive than the previously published value, which was obtained without close pH

¹⁵ F. A. Long, J. G. Pritchard, and F. E. Stafford, *J. Amer. Chem. Soc.*, 1957, **79**, 2362.

¹⁶ J. Koskikallio and E. Whalley, *Trans. Faraday Soc.*, 1959, **55**, 815.

control from only single kinetic results at two temperatures (*cf.* Table 2).¹⁵ The result for epichlorohydrin is the first, as far as we are aware.

TABLE 3

Arrhenius energies of activation (E_a)^a and entropies of activation (ΔS^\ddagger)^{a,b} for 25°

Oxide	$10^3 k_{H^+}/$ $l \text{ mol}^{-1} \text{ s}^{-1}$	$E_a/\text{cal mol}^{-1}$	$\Delta S^\ddagger/$ $\text{cal mol}^{-1} \text{ K}^{-1}$
Epichlorohydrin	8.32	$19,860 \pm 910$	-8.1 ± 3.2
Propylene oxide	47.9	$19,010 \pm 230$	-5.1 ± 0.8
Isobutylene oxide	6030	$19,340 \pm 230$	$+7.9 \pm 0.8$

^a The outside limits quoted for these values are derived with the assumption that the values of $\log k_{H^+}$ required may be in error by not more than ± 0.01 for propylene and isobutylene oxides and ± 0.04 for epichlorohydrin (*cf.* Table 1). ^b $\Delta S^\ddagger = 1.987 (2.303 \log k_{H^+} - 30.47) + E_a/298.2$.

DISCUSSION

Definition of Mechanisms.—Reactions in the specific acid-catalysis class are usually termed *A-1* if the reaction comprises steps like equations (3) and (4b), but *A-2* for (3) and (4a). It is observed empirically that all definitely established *A-1* and *A-2* reactions have, respectively, positive and negative entropies of activation.^{17,18} On this basis, the classification of our epoxide reactions would appear simple (*cf.* Table 3). However, some further consideration is called for, since the behaviour of some acid-catalysed reactions has driven authors, even in fairly recent chemical literature, to suggest concepts such as '... a borderline case between *A-1* and *A-2* reactions, but essentially an *A-2* reaction,'¹⁹ and '... the carbonium ions are captured by solvent before they are fully formed.'²⁰ Such ideas do not appear to be very helpful.

Our definitions of *A-1* and *A-2* are fairly straightforward and not unusual. With respect to Figure 1, the transition state may be assumed to have a higher free energy for the *A-2* case by virtue of a substantially lower entropy of activation than for the *A-1* case, the energies of activation being assumed to be more nearly the same (although this need not necessarily be so). The *A-2* mechanism is defined through a clearly bimolecular transition state such that the configuration of the carbon atom is inverted through nucleophilic attack at the back side of the ring. In the *A-1* case, a carbonium ion is formed which is isolated from the reaction products by a definite energy barrier, *H*, which may, however, be very low. If the barrier is relatively high, the carbonium ion will have time to reverse its configuration at the carbonium carbon atom many times before reaction is completed. If the barrier is critically low, in the limiting case the carbonium ion may not be able to complete one reversal before reaction is completed by nucleophilic attack *equally* at either side of the carbonium carbon atom. Thus, our definition is a conventional one depending on retention of configuration or racemisation in cases for which such optical phenomena may be

¹⁷ L. L. Schalegar and F. A. Long, *Adv. Phys. Org. Chem.*, 1963, **1**, 1.

¹⁸ E. Whalley, *Adv. Phys. Org. Chem.*, 1964, **2**, 93.

¹⁹ S. Sekiguchi, K. Matsui, and Y. Yasuraoka, *Bull. Chem. Soc. Japan*, 1970, **43**, 2523.

observed. Of course, it is possible that both *A-1* and *A-2* processes may occur to measurable extents concurrently if the value of *D*, the free-energy difference between the solvated epoxide conjugate acid and the bimolecular transition state on the one hand and the unimolecular one on the other, is small. With Gold,²¹ we do not see that it is necessary to suggest any mechanism that is intermediate between *A-1* and *A-2*.

In the absence of data on optically active epoxides, semi-empirical criteria may be examined to assess the role of water in this acid-catalysed hydrolysis: values of the entropy and volume of activation (ΔS^\ddagger and ΔV^\ddagger), and the relationships of reaction rates to the Hammett

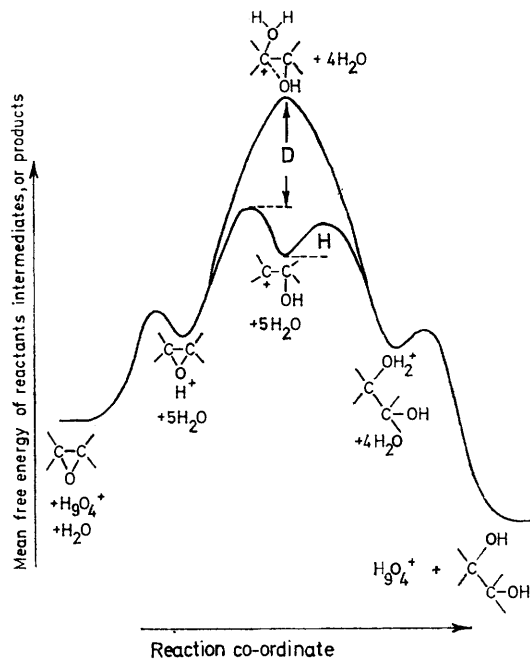


FIGURE 1 Illustration of the progress of *A-1* and *A-2* reactions

acidity function (H_0) and deuterium substitution in the solvent.

Epichlorohydrin.—Our value of ΔS^\ddagger for the acid-catalysed hydrolysis of epichlorohydrin is well within the negative range expected for the *A-2* mechanism. This result is supported by a ΔV^\ddagger of $-8.5 \text{ cm}^3 \text{ mol}^{-1}$,²² a value less than -2 being required for correlation with the *A-2* mechanism in general.^{16,18,23,24}

The linear variation of $\log k_{H^+}$ with $-H_0$ has a slope of 0.87 for the reaction of epichlorohydrin in aqueous perchloric acid solutions of concentration $>1M$.⁹ This value is nowadays interpreted in terms of the *A-2* mechanism, since the very thorough treatment of the subject by Bunnett relates slopes of *ca.* 0.9–0.8 or less to the *A-2* mechanism and slopes of *ca.* 1.0–1.1 or more

²⁰ W. L. le Noble, *Progr. Phys. Org. Chem.*, 1957, **5**, 207.

²¹ V. Gold, *J. Chem. Soc.*, 1956, 4633.

²² W. L. le Noble and M. Duffy, *J. Phys. Chem.*, 1964, **68**, 619.

²³ E. Whalley, *Trans. Faraday Soc.*, 1959, **55**, 798.

²⁴ R. J. Withey and E. Whalley, *Trans. Faraday Soc.*, 1963, **59**, 901.

to the *A*-1 mechanism.²⁵ (The slope of 0.87 was wrongly interpreted earlier as being sufficiently close to 1.00 to indicate a relationship to the *A*-1 mechanism, according to the original approximate form of the Zucker-Hammett hypothesis.^{9,26-28}) The *A*-2 correlation has been confirmed for rates of epichlorohydrin hydrolysis in aqueous nitric acid of concentration $>8M$, for which the variation of $H_0 + \log k_{H^+}$ with the log of the activity of water has a slope of $+1.7$ ²⁹ which corresponds to a slope of *ca.* 0.9 for $\log k_{H^+}$ against $-H_0$.²⁵ Thus, three criteria agree for epichlorohydrin.

In spite of advancements in the general theory of the deuterium isotope effect,³⁰⁻³³ the observed value $k_{D^+}/k_{H^+} = 1.89$ for epichlorohydrin⁸ cannot now be considered to distinguish between the *A*-1 and *A*-2 mechanisms in view of the wide variation of k_{D^+}/k_{H^+} values observed for the specific acid-catalysed hydrolysis of related compounds.³⁴

Propylene and Isobutylene Oxides.—The entropy and volume of activation for propylene oxide are both sufficiently negative ($-5 \text{ cal mol}^{-1} \text{ K}^{-1}$ at 25° and $-8 \text{ cm}^3 \text{ mol}^{-1}$ at 0°) for there to be no doubt as to an assignment of the *A*-2 mechanism by analogy with epichlorohydrin.^{16,18}

In the case of isobutylene oxide, our new value for the entropy of activation is $+8 \text{ cal mol}^{-1} \text{ K}^{-1}$ (25°), whereas the value for the volume of activation is $-9.2 \pm 1.7 \text{ cm}^3 \text{ mol}^{-1}$.¹⁶ In view of this, we have to consider why the entropy of activation for isobutylene oxide is positive, some 14 units more positive than for the slower-reacting epoxides, and also why the volume of activation is apparently so negative at the same time (next section).

Propylene and isobutylene oxides react too rapidly by the acid-catalysed path to be tested properly by the H_0 criterion at sufficiently high acid concentration, and no k_{D^+}/k_{H^+} values have been recorded for these oxides either.

General Nature of Epoxide Reactions in Relation to the Entropy of Activation for the Acid-catalysed Hydrolysis of Isobutylene Oxide.—Eliel's analysis of a large mass of data and various theories on the direction of ring opening in substituted ethylene oxide derivatives, including solvent effects thereon, has shown that although there is a definite argument to be made for more '*S_N1-like*' qualities in certain reactions, the bulk of them are plainly bimolecular as evident from the observation of inversion of configuration at the reaction centre.² (More '*S_N1-like*' means the favouring of a direction of ring-opening directed by the more stable carbonium ion that would be formed if the reaction could proceed unaided by the nucleophilicity of the reagent.)

Clear evidence for the operation of a unimolecular mechanism in acid-catalysed epoxide hydrolysis has only recently been forthcoming. When optically active (+)-(*R*)-styrene oxide is shaken with water acidified with perchloric acid, the resulting styrene glycol is completely racemised, which shows irrefutably the operation of the carbonium-ion mechanism (4b) in this case.³⁵ A number of earlier, but far less clear results for the addition of acids to styrene oxide and its substituted derivatives under diverse conditions have inferred the incursion of a unimolecular mechanism.³⁶

Mass spectrometric studies of the products of reaction of styrene oxide and *cis*- and *trans*-1-phenyl-1,2-epoxypropane with dilute aqueous perchloric acid enriched with $H_2^{18}O$ have shown that substitution by the nucleophile (water) occurs exclusively at the carbon atom which bears the phenyl substituent. Similar studies on 1-phenyl-2-methyl-1,2-epoxypropane have shown that the epoxide ring opens at the 1-carbon in the case of 55% of the molecules and at the 2-carbon for 45%.³⁷ Substitution of the epoxide ring by two methyl groups on the same carbon atom therefore leads to almost the same reactivity as substitution by one phenyl group, the latter having been shown to cause reaction through the unimolecular mechanism. Since it has been shown that the acid-catalysed hydrolysis of isobutylene oxide occurs with substitution exclusively at the substituted carbon of the epoxide ring,¹⁴ it may be strongly inferred in the above context that isobutylene oxide may react at least in part by the unimolecular mechanism defined above.

In view of the above facts, the value $+8 \text{ cal mol}^{-1} \text{ K}^{-1}$ for the entropy of activation of the acid-catalysed hydrolysis of isobutylene oxide appears quite acceptable. The energies of activation for acid-catalysed hydrolysis of propylene and isobutylene oxides agree to within *ca.* 300 cal mol^{-1} , *i.e.* to within the equivalent of $1 \text{ cal mol}^{-1} \text{ K}^{-1}$ (or *ca.* 800 cal mol^{-1} , $2.6 \text{ cal mol}^{-1} \text{ K}^{-1}$, at the outside). Thus, most of the difference in free energies of activation for reaction of these two molecules lies in the difference of *ca.* $13 \text{ cal mol}^{-1} \text{ K}^{-1}$ in the entropies of activation. The difference in entropies of solvation of propylene oxide and isobutylene oxide molecules is unlikely to be large, and the reaction of both molecules by *A*-2 paths should involve a difference in entropy of solvation of the transition states similar to that for the ground states. Hence, the observed difference in rates (factor of 110) and in entropies of activation may most plausibly be attributed to a mechanistic change from *A*-2 to *A*-1 in passing from propylene oxide to isobutylene oxide, attended by modification in entropy of solvation of the

²⁵ J. F. Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956, 4968, 4973, 4978.

²⁶ M. A. Paul and F. A. Long, *Chem. Rev.*, 1957, **57**, 1.

²⁷ L. Zucker and L. P. Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2791.

²⁸ F. A. Long and M. A. Paul, *Chem. Rev.*, 1957, **57**, 935.

²⁹ Z. A. Musharov, I. G. Kaufman, and S. G. Entelis, *Russian J. Phys. Chem.*, 1969, **43**, 47.

³⁰ E. L. Purlee, *J. Amer. Chem. Soc.*, 1959, **81**, 263.

³¹ C. G. Swain and E. R. Thornton, *J. Amer. Chem. Soc.*, 1961, **83**, 3884.

³² C. A. Bunton and V. J. Shiner, jun., *J. Amer. Chem. Soc.*, 1961, **83**, 3207.

³³ V. Gold, *Adv. Phys. Org. Chem.*, 1969, **7**, 259.

³⁴ P. M. Laughton and R. E. Robertson, in 'Solvent-Solute Interactions,' eds. J. F. Coetzee and C. D. Ritchie, Dekker, London, 1959, ch. 7.

³⁵ C. Dupin and J. F. Dupin, *Bull. Soc. chim. France*, 1970, 249.

³⁶ A. A. Akhrem, A. M. Moiseenkov, and V. N. Dobrynin, *Russian Chem. Rev.*, 1968, **37**, 448.

³⁷ H. E. Audier, J. F. Dupin, and J. Jullien, *Bull. Soc. chim. France*, 1968, 3850.

mechanistically different transition states. This occurs, obviously, through stabilisation of a tertiary carbonium ion centre in isobutylene oxide, because of the additional methyl substituent, so that a competitive reaction path of lower free energy of activation is established, as indicated in the above section on definition (Figure 1). Similar changes in mechanism with substituents have generally been known for a long time¹² and are increasingly documented.³⁸⁻⁴¹ Changes of medium can bring about similar mechanistic changes.^{41,42}

It does not detract from the above argument that styrene oxide and various of its substituted derivatives should undergo acid-catalysed ring-opening reactions in methanolic solutions with entropies of activation in the range -10 to -20 cal mol⁻¹ K⁻¹^{43,44} and predominant inversion of configuration.⁴⁵ The relatively low dielectric constant of methanol, compared to water, tends strongly to preclude the formation of free carbonium ions. Even in methanol, however, there appears to be 22% racemisation in the acid-catalysed methanolysis of styrene oxide,⁴⁵ which we would interpret in terms of concurrent *A-1* and *A-2* mechanisms. Furthermore, an *A-1* mechanism has been suggested for the acid-catalysed methanolysis of 1,1-diphenylethylene oxide owing to its relatively high entropy of activation of -0.6 cal mol⁻¹ K⁻¹.⁴⁶ In the same spirit, we note also that entropies of activation for BF₃-catalysed alcoholysis of isobutylene oxide are in the range -10 to -20 cal mol⁻¹ K⁻¹.¹⁹

Volumes of Activation.—Figure 2 summarises values of volumes and entropies of activation for a number of acid-catalysed hydrolyses,^{18,47,48} some reactions between hydroxide ions and neutral and charged substrates,⁴⁹ and diverse other reactions.⁵⁰ The mean scatter is not less than ± 5 units on both scales, and the point for isobutylene oxide is certainly not very exceptionally wide of the majority of the data points. Some of the general scatter may be due to differences in temperature, and it is possible that isobutylene oxide may show a more positive ΔV^\ddagger value at temperatures around 25°. In the consideration of this type of correlation, it has been pointed out that the volume change between initial state and transition state for both the reactant molecules and their solvent cages must be considered, the volume change for the latter depending markedly on attendant changes in electric field and charge distribution.^{51,52} An exact correlation between volumes and entropies of

activation is therefore not to be expected because these functions depend on charge distribution in different ways.⁴⁹ Certainly, the more that measurements on volumes of activation accumulate, the more anomalies and difficulties in interpretation appear to accompany general correlations.^{53,54} Nevertheless, ingenious arguments have been advanced, for example, as to why the observed volume of activation in the *A-2* acid-catalysed hydrolysis of ethyleneimine should be as high as *ca.* -2 cm³ mol⁻¹.^{48,53} The value of ΔV^\ddagger for acid-catalysed hydrolysis of isobutylene oxide may be considered

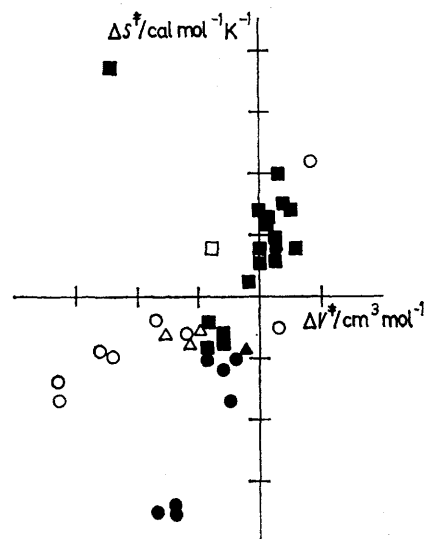


FIGURE 2 Entropies of activation plotted against volumes of activation for several acid-catalysed hydrolysis reactions (■)¹⁸ including those of isobutylene oxide (□), olefins (Δ),⁴⁷ and ethyleneimine (▲),⁴⁸ and for reactions in various other mechanistic classes (○)⁴⁹ and (●).⁵⁰ The axes cross at the point 0,0 and each scale is marked in divisions of 10 units

suspiciously low for an *A-1* case ($\gg -7.5$ cm³ mol⁻¹ at 0°). However, the *A-1* hydrolysis of an epoxide ring may involve overall contraction in volume on going through the transition state owing to slightly tighter solvation of the forming carbonium ion centre compared to the conjugate acid. This effect would not be as important to the entropy as the lack of transfer of a water molecule from the body of the solution to the *A-1* activated complex.

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