Mechanisms of Ring Opening of Oxirans by Acids in Aqueous and Non-aqueous Solvents

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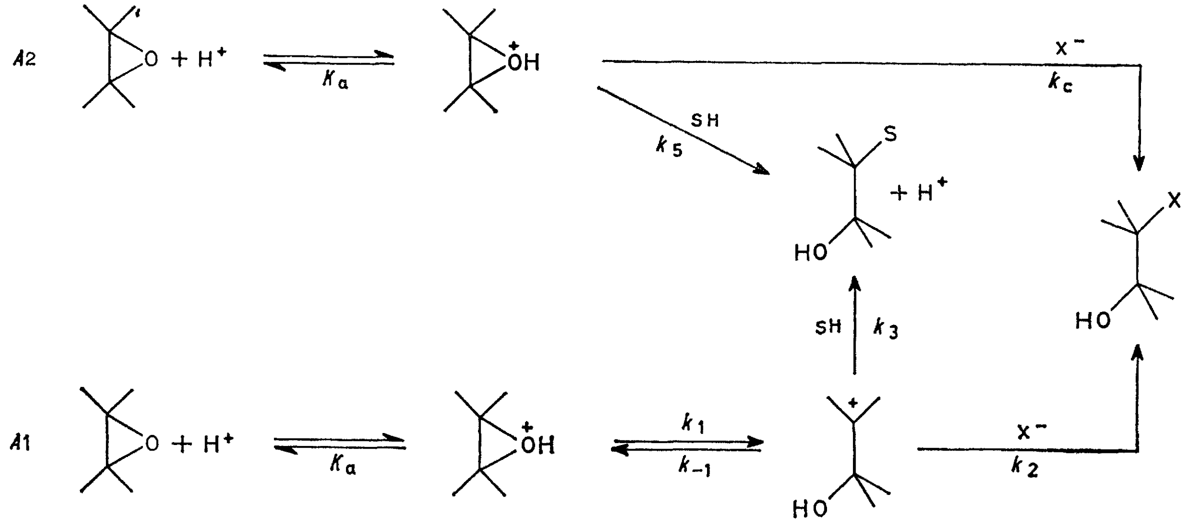
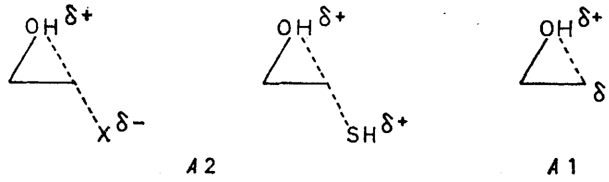
The kinetics of the ring opening of oxirans mainly by halogen acids in aqueous and non-aqueous solvents have been studied. Rate measurements and product proportions show that straightforward *A*1 or *A*2 mechanisms are insufficient to explain the facts. An ion-pair intermediate is proposed which rationalises many of the data.

It is generally agreed that oxirans (and likewise thiirans) open under acid conditions either by a bimolecular attack on the conjugate acid, or through the formation of a carbonium ion intermediate. The two extremes are *A*2 and *A*1 (Scheme 1).[1-3] The transition states corresponding to these two mechanisms are shown in Scheme 2. Ring opening of oxirans by halogen acids in aqueous organic solvents gives, in general, both halogenohydration and solvolysis, with the respective rate equations (1) and (2) for the *A*2 case and (3) and (4) for *A*1 where [e] is the concentration of oxiran. For solvolysis alone, as in perchloric acid catalysed hydration, the rates give the equation (5) for *A*2 and (6) for *A*1.



Scheme 1



Scheme 2

$$\text{d[halogenohydrin]/d}t = \frac{1}{K_a} k_c[\text{e}][\text{H}^+][\text{X}^-] \qquad (1)$$

$$\text{d[solvolysis product]/d}t = \frac{1}{K_a} k_s[\text{e}][\text{H}^+] \qquad (2)$$

$$\text{d[halogenohydrin]/d}t = \frac{1}{K_a}\cdot\frac{k_1k_2[\text{X}^-]}{k_{-1}+k_2[\text{X}^-]+k_3}([\text{e}][\text{H}^+]) \qquad (3)$$

$$\text{d[solvolysis product]/d}t = \frac{1}{K_a}\cdot\frac{k_1k_3}{k_{-1}+k_2[\text{X}^-]+k_3}([\text{e}][\text{H}^+]) \qquad (4)$$

$$-\text{d[e]/d}t = \frac{1}{K_a} k_s[\text{e}][\text{H}^+] \qquad (5)$$

$$-\text{d[e]/d}t = \frac{1}{K_a}\cdot\frac{k_1k_3}{k_{-1}+k_3}[\text{e}][\text{H}^+] \qquad (6)$$

The recent literature [1,2,4,5] shows that authors are not unanimous concerning the mechanism which prevails under given conditions. We thought that a systematic study of reactivity as a function of oxiran structure might lead to further insight into the problem. We have also tried to distinguish kinetically between the two mechanisms and have studied, in the first place, the chlorohydration and solvolysis of oxirans in 50% aqueous ethanol.

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[1] (*a*) J. Biggs, N. B. Chapman, A. F. Finch, and V. Wray, *J. Chem. Soc.* (*B*), 1971, 55; J. Biggs, N. B. Chapman, and V. Wray, *ibid.*, (*b*) p. 63; (*c*) p. 66; (*d*) p. 71.

[2] J. G. Pritchard and I. A. Siddiqui, 1973, *J.C.S. Perkin II*, 1973, 452.

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

[4] M. D. Carr and C. D. Stevenson, *J.C.S. Perkin II*, 1973, 518.

[5] V. J. Shiner, ' Isotope Effects in Chemical Reactions,' eds. C. J. Collins and N. S. Bowman, Van Nostrand, New York, 1971, p. 95.

Solvolysis and Chlorohydration of Aliphatic Oxirans in 50% *Aqueous Ethanol*.—Tables 1 and 2 give the rate constants of solvolysis by perchloric acid and chlorohydration by hydrochloric acid in 50% aqueous ethanol. In both cases, we note that the rate sequence is indicative of an S_N1 reaction of the conjugate acid but this cannot be fully affirmed because of the uncertainty in the values of the equilibrium constant K_a. Addy and Parker [6] interpret the rate sequences they obtained solely on the basis of the structural effect on the equilibrium constant of the $A2$ mechanism.

TABLE 1

Rate constants (min^{-1}) for the acid catalysed solvolysis at −9.80° of oxirans by 0.082M-perchloric acid in 50% aqueous ethanol determined by dilatometry

Oxiran	Solvolysis rate constant × 10^3	Relatives values
Ethylene oxide	0.073	1.0
	2.44 *	
2-Methyloxiran	11.4 *	4.65
trans-2,3-Dimethyloxiran	1.10	15.1
cis-2,3-Dimethyloxiran	2.38	32.4
2,2-Dimethyloxiran	35.5	484
Tetramethyloxiran	71.6	977
Cyclopentene oxide	0.518	7.07
Cyclohexene oxide	10.5	140
1-Methylcyclopentene oxide	44.2	605
1-Methylcyclohexene oxide	178	2 420

* Determined by direct titration of oxiran at −5° with 0.2M-$HClO_4$.

TABLE 2

Rate constants ($\text{min}^{-1}\ \text{mol}^{-2}\ \text{l}^2$) for the chlorohydration reactions of oxirans in 50% aqueous ethanol measured at 27°

Oxiran	Chlorohydration rate constant	Relative values
Ethylene oxide	4.94	1.0
2-Methyloxiran	12.7	2.57
trans-2,3-Dimethyloxiran	0.654 *	1.45
cis-2,3-Dimethyloxiran	2.35 *	5.2
2,2-Dimethyloxiran	89	18
	8.13 *	
Tetramethyloxiran	6.96 *	15.4
Cyclopentene oxide	9.88	2
Cyclohexene oxide	162	32.9
1-Methylcyclopentene oxide	58.2	11.8
1-Methylcyclopentene oxide	241	48.7

* Determined at 2°.

If the reaction goes partly by an S_N1 mechanism then the order towards chloride should be between zero and one; the overall experimental order will then be between two and three. In our experimental conditions solvolysis accompanies chlorohydration, which complicates the study of change of rate with varying concentrations of chloride ion. Therefore, a clear cut answer cannot be obtained in this way.

However, it is possible to calculate the rate constant for solvolysis from the measured chlorohydration rate and the independantly determined ratio [chlorohydration product] : [solvolysis product] which is given by expression (7) for the $A2$ case and (8) for $A1$. One may note that here the ratio does not involve the slow step, as the term $k_1/K_a(k_{-1} + k_2[X^-] + k_3)$ cancels out.

$$\int_{t=0}^{t=\infty} \frac{k_c[X^-]}{k_s} dt \qquad (7)$$

$$\int_{t=0}^{t=\infty} \frac{k_2[X^-]}{k_3} dt \qquad (8)$$

Further, it can be arranged experimentally that $[X^-]_0 \gg [e]_0$ so that $[X^-]$ may be considered constant. In these conditions k_c/k_s or k_2/k_3 are directly accessible to measurement by the evaluation of the aforementioned product ratio.

The hydration rate constant so calculated is then compared with that measured directly in the presence of perchloric acid. A complete analysis of the rate equations shows that these figures should be the same for an $A2$ mechanism and very different for a limiting $A1$ mechanism (that is when k_{-1} is very much smaller than $k_2[X^-]$ or k_3).

The experiments with tetramethyloxiran and 2,2-dimethyloxiran show that, within the limit of experimental error, the rate constants are the same. This test seems to favour an $A2$ mechanism if we consider only the usual classical mechanisms. This conclusion is not entirely convincing as it seems difficult to attribute to the equilibrium constant alone the fact that tetramethyloxiran (in which both carbons are tertiary and neopentyl-like) would react some 1 000 times faster than ethylene oxide, by a bimolecular mechanism.

Chlorohydration of Oxirans in Anhydrous Solvents.—*Rates*. It appeared of interest to look into the behaviour of oxirans in solvents where no solvolysis is possible. We treated the oxirans with HCl in anhydrous tetrahydrofuran (THF). Clean third order kinetics might be expected, but we found the results conformed to a second-order law. If a second-order law is assumed, doubling the HCl concentration results in only an insignificant change in rate constant, so the reaction is in fact second order. These constants are

TABLE 3

Second-order rate constants ($\text{min}^{-1}\ \text{mol}^{-1}\ \text{l}$) for chlorohydration of oxirans in THF at 0°

Oxiran	[Oxiran]/M	[HCl]/M	Rate constant *	Relative values
2-Methyl	0.05	0.05	0.31	1
	0.1	0.05	0.33	
	0.05	0.1	0.30	
2-Chloromethyl	0.05	0.05	0.012	0.04
	0.1	0.05	0.011	
	0.05	0.1	0.009	
2,2-Dimethyl	0.05	0.05	1.11	3.6
	0.1	0.05	1.18	
	0.05	0.1	1.00	
2-Phenyl	0.05	0.05	2.50	8.0
	0.1	0.05	3.10	
	0.05	0.1	2.20	
Cyclohexene oxide	0.05	0.05	4.86	12.4

* ±5%.

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[6] J. K. Addy and R. E. Parker, *J. Chem. Soc.*, 1965, 644.

given in Table 3. We investigated the effect of common and non-common ions, to examine salt effects. The results are given in Table 4. As we can see the addition of LiCl does not change the rate; this means that it is independent of chloride ion concentration.

Table 4

Second-order rate constants for the chlorohydration of 2-methyloxiran in 40 : 60 dioxan–ethanol

[Oxiran]/M	[Acid]/M	Added salts LiCl	Added salts $LiClO_4$	Rate constants (min^{-1} mol^{-1} l) *
0.033	0.033	0	0	1.05
0.033	0.067	0	0	1.01
0.067	0.033	0	0	1.11
0.033	0.033	0.033	0	1.15
0.033	0.033	0	0.033	1.20

* ± *ca.* 5%.

Product proportions. It is known that ring opening gives mainly the normal product for the aliphatic compounds.[3] These facts differ from our finding that in anhydrous solvents the chloride ion does not enter into the formation of the transition state. For this reason, we have measured the product proportions under the same conditions as used for the rate measurements. The results are given in Table 5. For the reactions in 50% aqueous ethanol, the determinations are effected by a kinetic method depending on the large differences in chlorohydrin solvolysis rates between the normal and abnormal products formed. In anhydrous solvents, the proportions are obtained by n.m.r. characterisation after concentration of the solution *in vacuo*. In both cases the precision may be estimated at ±5%.

Table 5

Product proportions for the chlorohydration of oxirans

Solvent	EtOH–H_2O 50 : 50	EtOH–Dioxan 60 : 40	THF	CH_3CN–C_6H_6 90 : 10
Oxiran				
2-Methyl	40	80	84	83
	60	20	16	17
2,2-Dimethyl	25		62	
	75		38	
2-Chloromethyl			100	100
			0	0
1-Methylcyclopentene oxide	31			
	69			
1-Methylcyclohexene oxide	59			
	41			

The first figures refer to % of normal product and the second to abnormal product.

The results obtained confirm those generally given in the literature.[3,6] A striking feature is the product proportion for 2,2-dimethyloxiran: in THF, where chloride ion does not participate, there is an excess of normal product; in aqueous ethanol where chloride does intervene there is a threefold excess of abnormal product.

Bromohydration of Oxirans in Anhydrous Ethanol.—At this point it appeared appropriate to study the kinetic behaviour of oxirans towards a different negatively charged nucleophile, also under anhydrous conditions. The bromohydration reaction was therefore investigated. The choice of solvent was dictated by experimental conditions. The high rate and the necessary use of conductivity measurements prohibit the use of THF as solvent; however we checked that there is no solvolysis product formed in absolute ethanol; the reaction was followed at −20°, a calibration plot of HBr concentration against conductivity having been established. The plots of hydrobromic acid concentration as a function of time fit neither a second- nor a third-order law.

We determined the order and the rate constant of the reaction using relationship (9). By taking several values

$$\log t = \log\frac{2^{\alpha-1}-1}{(\alpha-1)k} - (\alpha-1)\log a \qquad (9)$$

of the initial concentrations a, measuring the half-life times, $t_{1/2}$ the slope of the plot of log $t_{1/2}$ against log a gives $(\alpha - 1)$ and the intercept gives $\log[2^{\alpha-1}/(\alpha-1)k]$. It is possible, once the order α is known, to use the integrated rate equation and calculate k from the experimental points. We thus confirm the values of the rate constants obtained from the intercept.

The order is found to be overall 2.3; the rate constants and product proportions were found to be: 2 chloromethyloxiran 1.8 ± 0.01, 100% normal; 2 methyloxiran 56 ± 2, 81% normal, 19% abnormal.

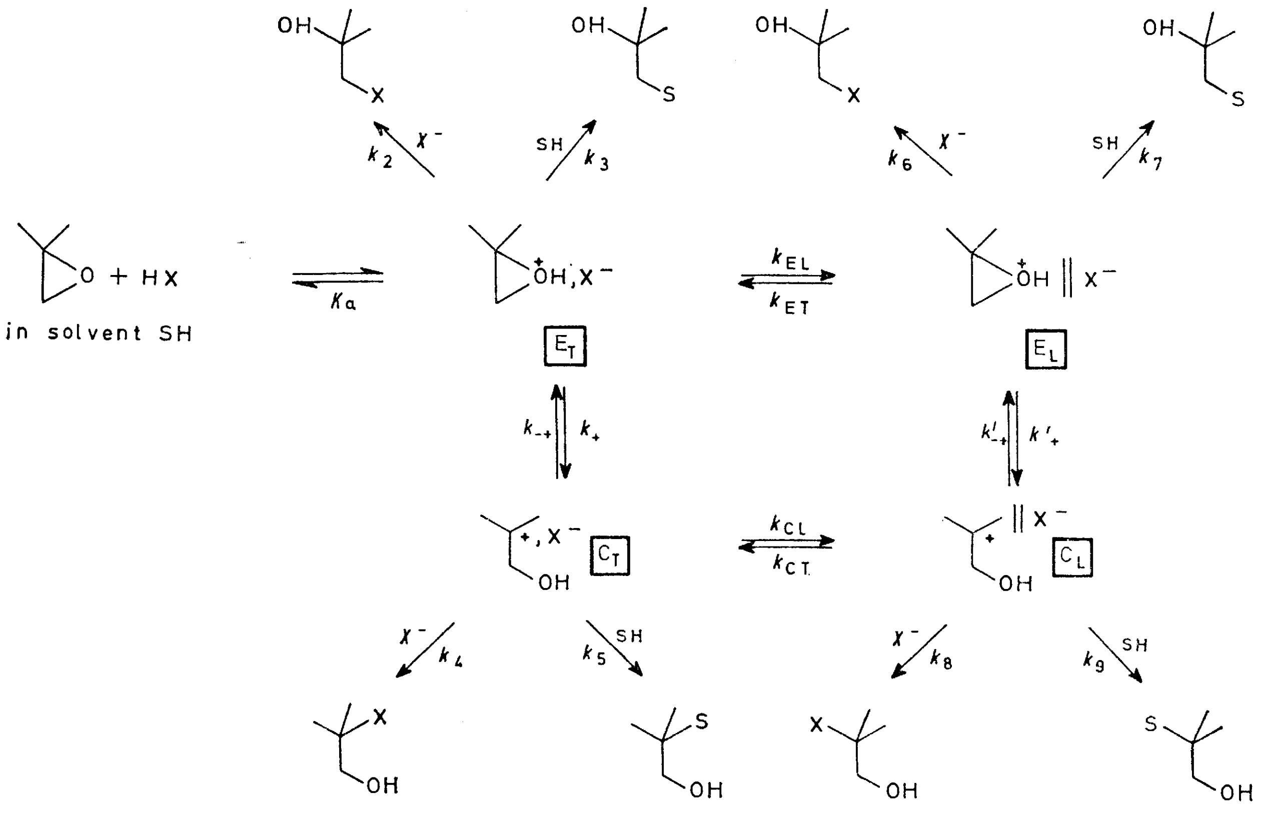
Non-integral orders of chemical reactions may arise if: (*a*) there are two competitive reactions of different integral orders; (*b*) a single reaction is going by two consecutive steps neither of which is truly rate-limiting: that is to say the energies, U, of the transition states are almost equal. One result above needs special comment: the reaction order and product proportions for 2-chloromethyloxiran; this compound gives exclusively normal product. It is hard to believe that this sole product could be formed by two competitive reactions of different order; this observation seems to favour possibility (*b*).

The study of oxiran reactions shows that the order depends on the nucleophile in comparable anhydrous solvents, but that this order also depends largely on the ionising power of the solvent, for the same nucleophile. The rate sequences with substitution are significant but the pre-equilibrium constant always makes a conclusion difficult.

DISCUSSION

The principal inconsistencies to note are the following: (1) the rate sequences go in the $A1$ sense; (2) product proportions imply the concurrent existence of both mechanisms, the $A2$ mechanism being generally preponderant; (3) the reaction order with respect to chloride ion in anhydrous solvents favours an $A1$ mechanism since chloride ion does not come in the transition state; (4) the mixed order and product proportion for the bromohydration reaction is consistent with neither mechanism but rather with a reaction having two consecutive rate-limiting steps.

We think that these apparently conflicting results can be explained if we admit that the reaction goes by the solvolytic Scheme 3, illustrated for the sake of convenience for 2,2-dimethyloxiran, first proposed by Winstein and his co-workers and developed by Shiner.[5] In Scheme 3 the first reaction is the rapid formation of the conjugate acid of the substrate leading to a tight ion pair, $\mathrm{E_T}$. This tight ion pair can react in several ways. (i) It can be attacked in a bimolecular manner by an anion $\mathrm{X^-}$ or by solvent (rate constants k_2 and k_3). (ii) It can also evolve to a second tight ion pair, $\mathrm{C_T}$, between a carbonium ion and the anion (k_{-+} and k_+); $\mathrm{C_T}$, in turn, can give products (k_4 and k_5) by nucleophilic attack. (iii) It can lead to a loose ion pair, $\mathrm{E_L}$ (k_{EL} and k_{ET}) which can in turn be attacked by nucleophiles (k_6 and k_7). $\mathrm{E_L}$ can also give a second loose carbonium ion pair, $\mathrm{C_L}$ (k'_+ and k'_{-+}). $\mathrm{C_L}$ Can also be formed directly from $\mathrm{C_T}$ (k_{CL} and k_{CT}) and lead to products by nucleophilic attack (k_8 and k_9).



Scheme 3

The only way we can explain our results for the chlorohydration of oxirans in anhydrous solvents (and also our previously published results on thiirans)[7,8] is to assume that k_{EL} is the rate-determining step, for in this case the kinetics are of second order for the oxirans (and thiirans)[7] and the product proportions will be governed by later, faster, steps.

The mixed order we find for the bromohydration of oxirans (also found previously for thiirans[7]) can be explained in two ways. (i) k_{EL} and $k_2[\mathrm{X^-}]$ are of the same order of magnitude so that the rate becomes partly dependent on $\mathrm{X^-}$ ($k_2[\mathrm{X^-}]$ being first order in halide). (ii) The energy barrier between $\mathrm{E_T}$ and $\mathrm{E_L}$ is lowered so that k_{EL} is increased and k_{TE} and $k_6[\mathrm{X^-}]$ become of the same order of magnitude. These are the two possibilities we have already mentioned above, and the 2-chloromethyl oxiran case pleads in favour of (ii).

In aqueous ethanol, where the rate is overall third order (first order in chloride ion), the rate-limiting steps are the bimolecular attacks on each individual intermediates, $\mathrm{E_T}$, $\mathrm{E_L}$, $\mathrm{C_T}$, and $\mathrm{C_L}$ (rate constants k_2, k_6, k_4, and k_8) by $\mathrm{X^-}$. The fact that we obtain considerable amounts of abnormal product shows that the reaction goes partly through one of the carbonium ions $\mathrm{C_T}$ or $\mathrm{C_L}$; the presence of $\mathrm{Cl^-}$ ions in the transition state indicates that the formation of these carbonium ions is not rate determining.

EXPERIMENTAL

Materials.—Ethylene oxide (Prolabo) had b.p. 12.5°. Propylene oxide (Fluka) had b.p. 35°.

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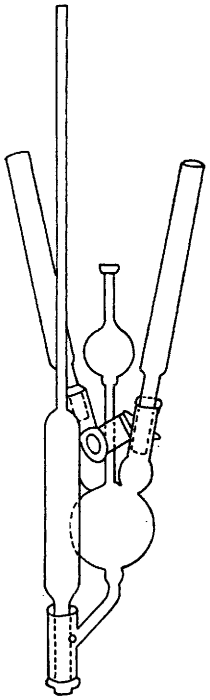
[7] A. Oddon and J. Wylde, *Bull. Soc. chim. France*, 1967, 1607.
[8] N. Schwartz, *J. Org. Chem.*, 1968, **33**, 2895.

2,2-*Dimethyloxiran*. The method of ref. 9 was employed.

cis- *and* trans-2,2-*Dimethyloxiran*. The corresponding alkenes (Dow) were treated by the technique of ref. 9 taking precautions to have as little dichloride as possible.

Tetramethyloxiran. This compound was obtained by Delacre's method [10] with slight improvements. Anhydrous pinacol was treated with dry HCl gas in benzene at reflux with a water separator. The formed chlorohydrin was vacuum distilled and treated with cold aqueous potassium hydroxide. The oxiran was extracted with ether and distilled, b.p. 90°. G.l.c. and i.r. showed that the product contains $<2\%$ pinacolone.

2-Chloromethyloxiran (Prolabo) had b.p. 114°. Epoxycyclohexane (Fluka) had b.p. 131°. Epoxycyclopentane, 1-methylepoxycyclopentane, and 1-methylepoxycyclohexane were graciously furnished by M. Mousseron-Canet (Directeur Scientifique, C.N.R.S.). All compounds were checked for purity by g.l.c. and n.m.r.



Apparatus for dilatometry

Analytical and Kinetic Methods.—Acid catalysed hydration rates of oxirans in 50% *water–ethanol.* 50% Water–ethanol refers to a mixture prepared by pipetting 50 ml of gas-free distilled water into a 100 ml measuring flask and topping up to 100 ml with 95% constant b.p. ethanol.

The dilatometric measurements were effected with the apparatus shown in the Figure. This device permits the two solutions, one of perchloric acid in 50% ethanol–water and the other of the oxiran in the same solvent, to be mixed rapidly before transfer to the dilatometer bulb. The temperature was kept constant to within 0.01°, checking with a Beckmann thermometer. A reference dilatometer of the same volume containing pure solvent was placed next to the measuring dilatometer. Readings were recorded on both dilatometers with a travelling microscope.

Analytical method. This uses the titration method of ref. 11. The only difference is that we used a pH meter to get a precise end point instead of an indicator.

Chlorohydration of Oxirans in Aqueous Ethanol.—The chlorohydration rate constants are measured by recording the disappearance of acid as the chlorohydrin is formed. Examination of equations (1) and (3) shows that this is feasible if $[Cl^-]_0$ and $[e]_0$ are in large excess with respect to $[H^+]_0$. Thus it can be shown that the record of the e.m.f. of a cell in which one half-cell is reversible to hydrogen ion will be a linear relation with time. The slope of this line leads to the experimental rate constant. A glass electrode in contact with the reaction mixture was used with an Ag–AgCl reference electrode dipped in N-KCl solution in aqueous ethanol connected to the reaction mixture by means of a KNO_3 bridge in aqueous ethanol. The solution was prepared by pipetting under nitrogen a known quantity of 1.52M-NaCl in 50% aqueous ethanol into the reaction vessel, then a known quantity of perchloric acid in the same solvent so that $[H^+]_0 = 0.01$M. The oxiran was injected by means of a syringe. Results are in Table 2.

Calculation of Solvolysis Rate Constants from Chlorohydration Rate Constants. Comparison with Extrapolated Measured Solvolysis Rate Constants.—The solvolysis rate constant when chlorohydration and solvolysis happen concurrently is (chlorohydration rate constant) $\times k_3/k_2$ by inspection of equations (1)—(4). It can be seen from equations (2) and (5) that the solvolysis rate constants for pure solvolysis *e.g.* by perchloric acid, and when chlorohydration accompanies solvolysis are the same for the *A*2 mechanism. Inspection of equations (4) and (6) shows they are different for the *A*1 case. If the reaction follows an *A*2 path, the solvolysis constant will be (experimental chlorohydration constant) $\times k_3/k_2$ $(= 6.96 \times 2.27 = 15.8$ min^{-1} mol^{-1} l for tetramethyloxiran). For *A*1 the solvolysis constant in the absence of chlorohydration is (experimental chlorohydration constant) $\times (k_3/k_2) \times (k_2[Cl^-]_0/k_3 + 1)$ $(= 6.96 \times 2.27 \times 1.67 = 26.5$ min^{-1} mol^{-1} for tetramethyloxiran). These figures must be compared with the constants measured for solvolysis alone. An extrapolation from measured rates of solvolysis, by perchloric acid assuming both a linear salt effect and the Arrhenius relationship gives a value of 14.5 ± 2.7 min^{-1} mol^{-1} l for the solvolysis rate for tetramethyloxiran at the same temperature and ionic strength as used in the chlorohydration experiment.

A test has also been carried out for 2,2-dimethyloxiran. The value of the solvolysis rate as calculated from the chlorohydration rate, gives a value of 27 for a typical *A*1 case, and 18 min^{-1} mol^{-1} l for an *A*2 or a non-typical *A*1 case. Account has been taken for product proportions so that the test applies only to the tertiary carbon atom. The value of the extrapolated solvolysis rate is 17.5 ± 3.0 min^{-1} mol^{-1} l.

Chloro- and Bromo-hydration of Oxirans in Non-aqueous Solvents.—Chlorohydration in dioxan–ethanol and THF was followed by titration. The acid solution and the oxiran solution were mixed in a thermostatted Kjeldahl flask. Portions of the solution were rapidly pipetted into a solution containing sufficient dilute NaOH to neutralise the initial acid. The excess of NaOH is titrated with acid to determine the remaining acid, and hence the oxiran.

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[9] C. E. Wilson and H. J. Lucas, *J. Amer. Chem. Soc.*, 1936, **58**, 2396.

[10] M. Delacre, *Bull. Soc. chim. France*, 1908, 1586.

[11] M. Mousseron, J. Jullien, and A. Peyron, *Bull. Soc. chim. France*, 1956, 1093.

To prevent the reverse reaction, the titration is done in highly dilute solution and it is possible to check the elimination of the reverse reaction by doing titrations at intervals.

For bromohydration a standardisation curve was obtained for conductivity as a function of concentration of 0.01—0.05M-HBr in anhydrous ethanol. Using the same cell, oxiran and HBr were allowed to react, and the conductivity as a function of time was recorded, and with the calibration curve the acid concentration at a given time was determined.

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