359. *The Chemistry of Ethylene Oxide. Part IV.* The Kinetics of the Reaction of Ethylene Oxide in Pyridine Solutions of Hydrogen Halides.*

By A. M. Eastham.

Ethylene oxide reacts with pyridine solutions of hydrogen halides to yield halogenohydrin and 2′-hydroxyethylpyridinium halide. A kinetic investigation of the reaction at 25° indicates that the dependence of the rate upon acid concentration decreases from second order to first order as the acid concentration increases, while simultaneously the proportion of halogenohydrin in the product increases. The change in order is attributed to a change in mechanism due to the association of the ions to form ion-pairs. The mechanism based on ion-pairs will also account for the facts that acids such as perchloric and nitric do not have identical catalytic activity in pyridine solutions and that in mixtures of acids the acids behave independently.

Studies of hydrogen chloride–lithium chloride solutions suggest that these two chlorides catalyse the reaction of ethylene oxide with pyridine in essentially similar fashion. The rate constant for hydrogen chloride is about seven times that for lithium chloride.

In previous papers we reported the results of studies on the reaction of ethylene oxide with amines in aqueous and in pyridine solutions (Eastham, Darwent, and Beaubien, *Canadian J. Chem.*, 1951, **29**, 575, 585). Although the reaction takes the general form

$$R_3N + \underbrace{CH_2{-}CH_2}_{O} + H^+ \longrightarrow R_3N^+{\cdot}CH_2{\cdot}CH_2{\cdot}OH$$

it was found to be independent of the proton source over the pH range 4—14 in aqueous solutions containing ammonium-type ions. No specific hydrogen-ion-catalysed reaction

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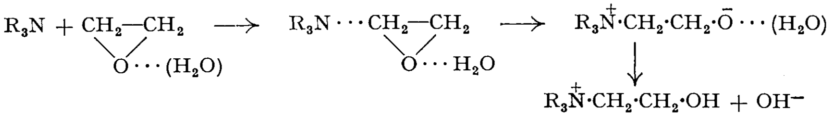
* Part III, *Canad. J. Chem.*, 1951, **29**, 585.

was observed although from analogy with other ethylene oxide reactions one would be expected; our failure to find it was perhaps due to the fact that appreciable concentrations of both hydrogen ion and free amine cannot be obtained in the same solution.

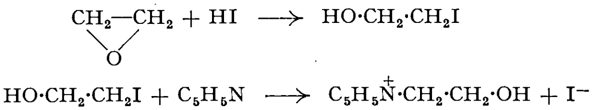
The results of the experiments in aqueous solution seem to indicate that water, through hydrogen bonding and/or solvation, plays an important part in the reaction and suggests a mechanism of the following type,



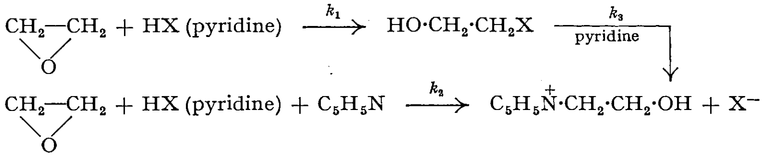
in which the rate-controlling step, the rupture of the C–O bond, is essentially an ionization process. Such an ionization would be assisted on the one hand by the high dielectric constant and solvating activity of water (cf. Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185), and on the other by the ability of nitrogen to form a positive ion.

In anhydrous pyridine solution, with pyridine acting as both solvent and reactant, the reaction was found to be strictly dependent upon the hydrogen-ion concentration, a fact readily explained on the basis of the above mechanism. More difficult to interpret, however, was the observation that when the hydrogen ion was supplied as the pyridinium salt of a strong acid the reaction rate was, qualitatively, proportional to the strength of the undissociated acid; for instance, perchloric acid was about twice as effective as sulphuric and three times as effective as nitric acid in promoting the reaction. Now in a solvent as basic as pyridine, where complete ionization of strong acids must be assumed, the proton source in all cases is presumably the pyridinium ion and therefore the acid anion must either modify the pyridinium ion or else must participate directly in the reaction mechanism. The latter alternative seemed unlikely since the addition of sodium perchlorate to the perchloric acid-catalysed reaction had no effect upon the rate, and we therefore concluded that the anion must influence proton availability.

However, it was also observed that when hydrogen iodide was employed as the proton source, the reaction occurred, at least in part, in two quite definite steps, which could be represented by the following simplified equations:



The final product, like that obtained from perchloric acid, is a 2′-hydroxyethylpyridinium salt but its formation in this case involves participation of an anion in the reaction mechanism. It seems unlikely that such participation occurs in the case of the perchlorate ion, and therefore in the presence of halogen acids two separate reactions must lead to the formation of the 2′-hydroxyethylpyridinium salts, *i.e.*,



In the case of hydrochloric acid k_3 is relatively small, and both primary processes may therefore be investigated by following simultaneously the disappearance of hydrogen and chloride ions. A study of these reactions was therefore undertaken with the object of obtaining further information on the reaction mechanism, particularly with respect to the role of the anion.

EXPERIMENTAL

Materials.—(a) *Pyridine.* Both fresh and recovered pyridine were employed and were prepared for use in the following manner. The pyridine was kept for several days over solid potassium hydroxide, then refluxed for a few hours and distilled. The distillate was carefully fractionated to remove most of the remaining water and other low-boiling materials and kept for a day or two with anhydrous aluminium chloride. It was distilled from the aluminium chloride and, finally, carefully fractionated.

(b) *Pyridinium halides.* Pyridinium iodide and bromide were prepared as the crystalline salts by neutralizing the corresponding acids with pyridine and isolating and recrystallizing the products. The bromide was rather hygroscopic but was readily dried at 100°. The dry salts were analysed by titration with standard sodium hydroxide to a potentiometric end-point and found to contain not less than 99·7% of the theoretical amount of acid. Solutions of these salts were then prepared from weighed samples.

Pyridinium chloride was too hygroscopic for easy handling so was prepared as its pyridine solution. Gaseous hydrogen chloride was passed through sulphuric acid scrubbers and the dry gas absorbed in pyridine (solubility about 7 g./l.). The concentration of the solution was then determined by titration as described below.

Analyses.—Reaction mixtures were prepared and sampled as described in Part III (*loc. cit.*) and analysed according to the following procedure. A sample (10—50 c.c., but preferably about 20 c.c.) was transferred to a 125-c.c. long-necked flask and connected to a vacuum system by a ground-glass joint. The pressure was rapidly reduced to about 1 mm. and the time recorded at the onset of rapid ebullition, as most, if not all, of the ethylene oxide is removed at this point. The sample was then evaporated just to dryness at temperatures below 30°. Great care was necessary in evaporating the bromide solutions for the pyridinium bromide forms a flaky residue which may be carried through the long neck. Best results were obtained by shaking the flask so as to keep the precipitate wet until most of the pyridine had been removed.

The dry residue was taken up in about 25 c.c. of carbon dioxide-free water and titrated with carbonate-free alkali, the end-point being determined potentiometrically. The normality of the alkali was usually such that 5—6 c.c. were required for a sample at zero time and the titrations were reproducible and accurate to about $0 \pm 0{\cdot}02$ c.c. even with acid solutions as dilute as 0·001M. With very dilute solutions good end-points were obtained only when all excess of pyridine had been carefully removed from the sample.

On completion of the acid–base titration, the free pyridine in the solution was neutralized by adding 0·5M-perchloric acid to a pH of 3·8—4·0. The chloride ion was then determined by titration with standard silver nitrate solution by use of dichlorofluorescein (Kolthoff, Lauer, and Sunde, *J. Amer. Chem. Soc.*, 1929, **51**, 3273). The error in this titration was about 1% and on solutions of hydrogen chloride or hydrogen bromide the results were in excellent agreement with those obtained by acid–base titration.

The methods of analysis were tested on synthetic mixtures of hydrogen chloride and ethylene chlorohydrin in pyridine and found to be satisfactory.

Reaction Products.—In the reaction of ethylene oxide with pyridine solutions of hydrogen chloride, two principal products are formed, ethylene chlorohydrin and 2′-hydroxyethylpyridinium chloride: the latter is precipitated as a white crystalline salt at rather low concentrations and reactions cannot therefore be carried very far. The corresponding bromide and iodide are more soluble.

The crystalline product from a number of reactions was accumulated and washed thoroughly with pyridine. It was taken up in a minimum quantity of absolute methanol, the solution diluted with pyridine, and the product slowly precipitated with dioxan as fine, needle-like crystals (Found: C, 52·7; H, 6·07; Cl, 22·1. Calc. for $C_7H_{10}ONCl$: C, 52·6; H, 6·28; Cl, 22·2%).

Since ethylene chlorohydrin reacts with pyridine on heating and therefore cannot be separated by distillation, it was identified in the following manner. An excess of ethylene oxide was added to 50 c.c. of 0·18N-hydrogen chloride in pyridine and set aside for 24 hours. The mixture was then distilled at room temperature under vacuum. A small fore-run containing unreacted ethylene oxide was discarded, and the remainder collected at −70° with precautions to prevent the condensation of moisture in the solution. The distillate was then treated with sufficient α-naphthyl *iso*cyanate to react with all the chlorohydrin and kept for sixteen hours. A small precipitate of di-α-naphthylurea was filtered off, and the solution evaporated to dryness under vacuum. The residue was taken up in boiling hexane, and the solution filtered, concentrated, and cooled. The thread-like crystals which separated were shown by mixed m. p. determination to be identical with the urethane prepared from pure chlorohydrin; the yield of crude product was 1·2 g. (50% based on hydrogen chloride), and the m. p. 95—98°, and 99—100° after recrystallization from hexane.

Reaction of Ethylene Chlorohydrin with Pyridine.—An estimate of the rate at which ethylene chlorohydrin is converted into 2′-hydroxyethylpyridinium chloride was obtained by preparing solutions of the chlorohydrin in pyridine and determining the rate of formation of chloride ion. The first-order rate constant thus obtained was approximately 3 × 10^{-5} min.$^{-1}$ at 25°, a value too low to have any significant effect on the composition of the reaction products. This constant was not influenced by addition of small amounts of hydrogen chloride.

TABLE 1.

Acid	Oxide							
0·0353 HCl	0·0565	Reaction, %	10	15	19	22	27	32
		Chlorohydrin, %	74	65	65	68	65	63
		10^3k	11·9	12·2	12·2	12·1	12·2	12·0
0·0685 HCl	0·0685	Reaction, %	16	21	28	36		
		Chlorohydrin, %	66	66	68	67		
		10^3k	13·3	13·3	13·3	13·4		
0·00919 HBr	0·0263	Reaction, %	24	38	46	54	67	
		Bromohydrin, %	77	81	80	78	71	
		10^3k	79·4	78·8	78·7	77·0	77·1	
0·0506 HBr	0·0682	Reaction, %	23	40	55	63		
		Bromohydrin, %	90	89	84	81		
		10^3k	83·2	81·2	81·2	81·0		
		Reaction, %	25	40	55	65	75	
0·00385 HI	0·0239	10^3k	195	189	192	188	187	
0·00977 HI	0·0283	,,	227	222	—	218	214	
0·0604 HI	0·0602	,,	255	253	249	—	248	

Data.—All experiments were performed at 25·0° in a bath controlled to 0·005°. All rate constants recorded, unless otherwise stated, are second-order constants expressed as mole^{-1} l. min.$^{-1}$ and calculated from the expression d[products]/dt = k[oxide][acid] on the assumptions that one molecule of oxide disappears with one molecule of acid, and that $k = k_1 + k_2$.

FIG. 1.

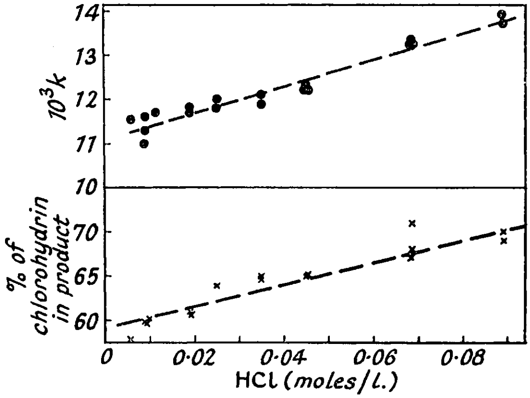
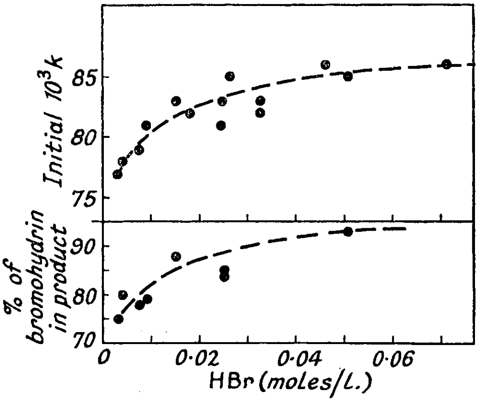


FIG. 2.



For the hydrogen chloride reactions where no deviations from second order were observed, the rate constants were obtained in the usual way by plotting the data and obtaining the best straight line through the points. With the bromide, and more especially with the iodide, where deviations from second order were observed, the rate constants were calculated for each point and plotted against the percentage reaction. The initial rate was then estimated by extrapolation to zero reaction. Some typical runs for each acid are shown in Table 1, where concentrations of acids and of ethylene oxide are given in moles/l.

Results.—The data for the reaction of ethylene oxide in pyridine solutions of hydrogen chloride are shown in Table 2 and Fig. 1. They are perhaps somewhat more accurate than the corresponding data for the bromide and iodide because, experimentally, the individual chloride reactions follow a strict second-order course and because chlorohydrin is relatively stable in pyridine. Actually, since the rate constant shows an increase with increasing hydrogen chloride concentration, deviations from second order might be expected but none was observed, probably because the precipitation of 2′-hydroxyethylpyridinium chloride prevented the reactions being carried beyond about 40% conversion. The percentage of chlorohydrin in the reaction product remained constant, within experimental error, over the course of the run.

TABLE 2.

HCl (in moles/l.)	Oxide (in moles/l.)	10^3k*	Chlorohydrin in product, %	HCl (in moles/l.)	Oxide (in moles/l.)	10^3k *	Chlorohydrin in product, %
0·1115	0·1355	14·4	—	0·0353	0·0565	12·1	65
,,	0·0892	14·2	72	,,	0·0562	11·9	65
0·0890	0·0766	13·9	69	0·0187	0·0565	11·7	61
,,	0·0674	(13·7)	70	,,	0·0377	11·8	61
0·0685	0·0910	13·3	67	0·0113	0·0487	11·7	—
,,	0·0692	13·3	71	0·00915	0·0367	11·6	60
,,	0·0444	13·3	68	,,	0·0232	11·3	60
0·0447	0·0791	12·2	65	0·00880	0·0334	11·0	60
,,	0·0533	12·2	65				
,,	0·0277	12·3	(63)				

* In l. mol.$^{-1}$ min.$^{-1}$.

The data for the reactions with hydrogen bromide and iodide are shown in Figs. 2 and 3. No attempt was made to determine iodohydrin because it reacts rapidly with pyridine; for the same reason the bromohydrin determinations may be slightly low.

FIG. 3.

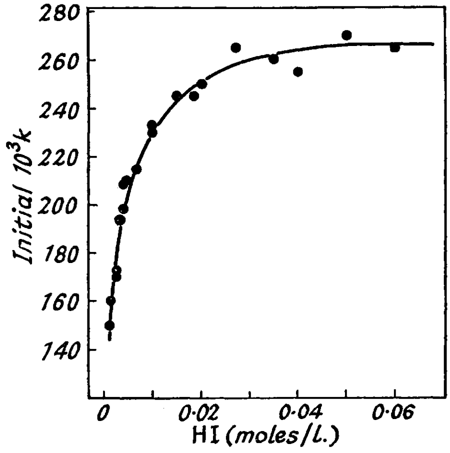
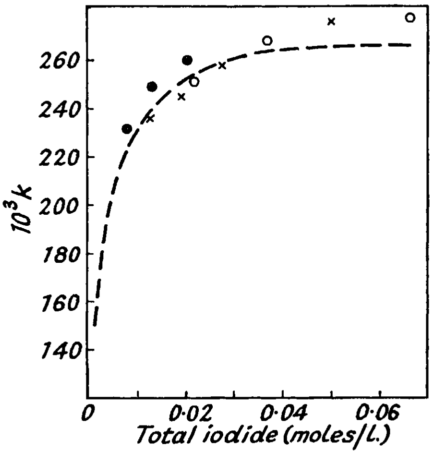


FIG. 4.



—— HI *alone* (*from Fig.* 3). ● 0·00275M-HI.
× 0·0051M-HI. ○ 0·010M-HI.

It is apparent that the strict first-order dependence on acid concentration observed with perchloric and other " inert " acids has given way in the case of halogen acids to a dependence which seems to decrease from second to first order as the acid concentration is increased. The interpretation of this change in order obviously requires further information on the effect of (*a*) halide ions and (*b*) ionic strength on the reaction rate.

The only alkali halides readily soluble in pyridine are the lithium salts and sodium iodide. Unfortunately, however, the addition of lithium chloride to hydrogen chloride solutions gave rates which suggested that the lithium ion behaved like a proton, and the study of halide-ion effects was therefore restricted to the sodium iodide–hydrogen iodide system. The results with lithium chloride are considered separately (see p. 1943).

In Fig. 4, the observed second-order rate constants, calculated from the disappearance of *acid* in the solution, are plotted against the total iodide-ion concentration for various mixtures of sodium iodide and hydrogen iodide. It is seen that *k* varies with the total iodide rather than with the hydrogen iodide concentration and it is therefore not surprising that the deviations from second order (Table 1) almost disappear in the presence of relatively large amounts of sodium iodide, since under these conditions the iodide-ion concentration remains essentially constant throughout the reaction.

The increase in the rate constant thus seems to be related either to the iodide-ion concentration or to the ionic strength. The investigation of ionic strength effects in solvents of low dielectric constant, however, is difficult, apparently because the reactive entities are not ions, but ion-pairs. For example, when sodium perchlorate is added to a pyridine solution of hydrogen iodide, an equilibrium between ion pairs is set up: $C_5H_5N,HI + NaClO_4 \rightleftharpoons NaI + C_5H_5N,HClO_4$, and our evidence suggests that such equilibria move in the direction which favours the association of the smallest negative with the smallest positive ion (Eastham and Jeffrey, unpublished). Now the total iodide-ion concentration in the solution remains unchanged as a result of the above equilibrium, and hence from the point of view of the data of Fig. 4, the significant change is the substitution of perchloric acid for a part of the hydriodic acid. Perchloric acid is, however, at least as strong an acid as hydriodic and one might therefore expect that the rate of disappearance of ethylene oxide would be, if anything, increased by the addition of sodium perchlorate. Actually, however, the rate was very sharply decreased, which leads to the conclusion that the hydriodic and perchloric acids act independently according to their individual rate constants of 200×10^{-3} and 24×10^{-3}, respectively.

It is evident, then, that in such solutions there are no "neutral" salts and hence that salt effects cannot be investigated directly. It seemed possible, however, that by studying mixtures of acids one might be able to obtain some information both on ionic-strength effects and on the extent of independent behaviour of acids. Rate studies were therefore made on solutions containing mixtures of hydriodic and perchloric acids and hydriodic and nitric acids, in the presence of excess of ethylene oxide. Now if the two acids behave independently, the contribution of the nitric or perchloric acid to the overall rate will be small, and may be estimated fairly accurately from the respective rate constants, $7{\cdot}41 \times 10^{-3}$ and $23{\cdot}9 \times 10^{-3}$; the contribution of the hydrogen iodide may then be obtained and should yield a rate constant corresponding to a value obtained from Fig. 3 either at the same iodide concentration or at the same ionic strength. Measurements were made in the initial stages of reaction only, in order to simplify the calculations and to minimize the introduction of new ionic equilibria by the 2′-hydroxyethylpyridinium salts formed during the reaction. The results of these experiments are shown in Table 3. The results for mixtures of nitric and hydriodic acids are evidently in excellent agreement with the view that the rate of the iodide reaction is determined by the iodide-ion concentration rather than by the ionic strength, but unfortunately the results with perchloric acid fail to confirm them. It does seem clear, however, that the acids act essentially independently of each other, and hence that the reactive species are ion-pairs, or some other associated form of the acid.

TABLE 3.

HI (moles/l.)	HNO_3 (moles/l.)	Oxide (moles/l.)	$10^3k_{HNO_3}$ (assumed)	10^3k_{HI} (obs.)	10_3k_{HI} from Fig. 3 at equivalent ionic strength	10_3k_{HI} from Fig. 3 at equivalent $[I^-]$
0·00356	0·00376	0·0311	7·4	197	222	192
0·00354	0·00366	0·0262	7·4	190	219	190
HI	$HClO_4$	Oxide	$10^3k_{HClO_4}$			
0·00331	0·00255	0·0362	23·9	232	210	188
0·00371	0·00344	0·0305	23·9	241	218	195
0·00385	0·00495	0·0305	23·9	228	225	195

DISCUSSION

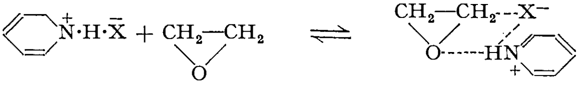
A mechanism of the type

$$\begin{array}{rrcll} & \text{Oxide} + H^+ & \rightleftharpoons & \text{Oxide},H^+ & (a) \\ & \text{Oxide},H^+ + I^- & \longrightarrow & HO{\cdot}CH_2{\cdot}CH_2I & (b_1) \\ \text{or} & \text{Oxide},H^+ + C_5H_5N & \longrightarrow & HO{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5 & (b_2) \end{array}$$

has been suggested by King, Berst, and Hayes (*J. Amer. Chem. Soc.*, 1949, **71**, 3498) to explain the formation of 2′-hydroxyethylpyridinium salts in pyridine solutions of hydrogen iodide; it is basically similar to the type of mechanism usually postulated for the reactions of ethylene oxide in aqueous solutions (Hammett, "Physical Organic Chemistry," McGraw-Hill, 1940). Such a mechanism would account for the shape of the curves in Figs. 3 and 4 if, with increasing iodide-ion concentration, step (b_1) becomes relatively very rapid so that the rate-controlling step shifts from (b) to (a). The dependence of the rate of process (b_2) upon the acid strength of the anion would then have to be attributed to a variation in the equilibrium constant of step (*a*), *i.e.*, a sort of general acid catalysis, but (see also Part III, *loc. cit.*) this view is not without objections, the most serious being that it does not permit an explanation of the independent behaviour of acids in mixtures, or of the marked decrease in rate which occurs when sodium perchlorate is added to a pyridine solution of hydrogen iodide. In addition, it may be noted that on the basis of this mechanism it is merely fortuitous if the reaction acquires second-order kinetics at the point where halogenohydrin becomes the exclusive product of the reaction.

It seems therefore that the mechanism as written can hold only for those very dilute solutions where dissociation into individual ions is high and where, experimentally, the reaction shows third-order kinetics. It can, however, be modified to cover most of the experimental data if one supposes that the change in kinetic order with increasing halide-ion concentration reflects not so much a change in mechanism as a change in the ionic character of the solutions. The fully ionic mechanism (above) then gives way at higher concentrations to a mechanism in which the kinetic entities are not ions, but ion-pairs.

The first step in such a mechanism would be the rapid formation of a complex :



Reaction would then proceed through the slow decomposition of this complex either by rearrangement to halogenohydrin or by attack of solvent molecules at carbon, both processes being experimentally of the second order. The essential change which takes place with increasing concentration is thus presumed to be a closer association of the anion with the complex.

It seems necessary to suppose that an electrostatic association exists between the carbon and the anion, which so disturbs the polarity or resonance of the oxide ring that the susceptibility of the oxide to solvent attack is altered. This assumption follows from the fact that it is the basicity rather than the size of the anion which determines the rate, and hence that the effect is electronic rather than steric.

If this hypothesis is correct, then at some low concentration where dissociation of the ions is complete, the formation of 2′-hydroxyethylpyridinium salts should occur at identical rates with all strong non-nucleophilic acids. Little evidence is available on this point but it was noted in the earlier work that the rates with sulphonic acids do seem to show an upward trend at low concentrations whereas those with nitric acid do not. Since dissociation effects would be greatest with the largest ions, these very incomplete data may provide some support for our view.

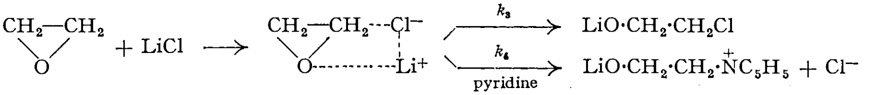
The close association between the anion and carbon, as postulated above, would be expected to increase the rate of nucleophilic attack by the ion and to lead to a maximum rate when association of the ions is complete. With active ions such as bromide and iodide this region of maximum rate should also be a region of almost exclusive halogenohydrin formation, as is observed. With the less active chloride ion one might expect both the rate and the ratio of products to be constant over the whole experimental range, since chlorides dissociate less readily than do the bromides and iodides. In practice, however, as the chloride-ion concentration is increased, both the rate and the proportion of chlorohydrin in the product increase slowly. No satisfactory explanation for this rise has been obtained.

Some support for the views expressed here can be obtained from the dissociation constants of alkali iodides in pyridine solutions at 25° (Burgess and Kraus, *J. Amer. Chem. Soc.*, 1948, **70**, 706), since the evidence suggests that pyridinium and sodium salts are not greatly different in their dissociations. From the constant it may be estimated that sodium iodide is about 25% dissociated at 0·001M-, and 10% at 0·01M-concentration; the levelling off of the curve in Fig. 3 at about 0·03M is therefore in good agreement with these data. It follows that the effect of sodium iodide on the rate (Fig. 4) can be readily interpreted as a common-ion effect.

Also relevant is the work of Walvekar, Phalnikar, and Bhide (*J. Indian Chem. Soc.*, 1943, **20**, 131) on the fission of aromatic ethers by halogen acids. These authors report that cleavage of the ethers by un-ionized acids in carbon tetrachloride solution is very slow, but is greatly accelerated by the addition of a small amount of pyridine.

Catalysis of the Reaction of Ethylene Oxide with Hydrogen Chloride by Lithium Chloride.—In an effort to determine whether the increase in the rate of reaction described on p. 1939 was due to the increase in chloride-ion concentration, lithium chloride was added to the reaction mixtures, and the rate of acid disappearance determined. It was found that the rate constant, calculated on the assumption of first-order dependence on both acid and oxide, increased steadily throughout the reaction; the deviation was most marked at high ratios of lithium chloride to hydrogen chloride. This behaviour was in distinct contrast to the effect of sodium iodide on the reaction of ethylene oxide with hydrogen iodide, for there the sodium iodide, apparently by maintaining a relatively constant concentration of iodide ion, had the effect of suppressing deviations from second order.

The results suggested that the lithium chloride was participating directly in the reaction. Now it is known (Rheinbodt, Luyken, and Schmittmann, *J. pr. Chem.*, 1937, **148**, 81) that lithium halides, in contrast to the alkali and ammonium halides, form stable oxonium compounds with dioxan. The ethylene oxide molecule in all probability is structurally quite similar to dioxan, and might therefore form similar complexes, which in turn would presumably resemble the ethylene oxide–pyridinium salt complexes postulated earlier as the reactive intermediates in the reaction between oxide and acids. We may therefore consider the possibility of a reaction of the following form:



Such a mechanism is exactly analogous to that postulated earlier but in the presence of hydrogen chloride would be followed immediately by a rapid exchange reaction, *i.e.*,

$$\mathrm{LiO{\cdot}CH_2{\cdot}CH_2X + HCl \longrightarrow HO{\cdot}CH_2{\cdot}CH_2X + LiCl}$$

The net effect therefore would be a more rapid disappearance of both oxide and acid, in agreement with the experimental data.

On this basis we may set up the following rate expression for the reaction,

$$\mathrm{d[products]/d}t = k_5\mathrm{[oxide][HCl]} + k_6\mathrm{[oxide][LiCl]}$$

If a, b, and c are the initial concentrations of oxide, acid, and lithium chloride, respectively, and if x and y are the amounts of oxide disappearing, in time t, by the respective mechanisms, then

$$\mathrm{d}(x + y)/\mathrm{d}t = k_5(a - x - y)(b - x - y) + k_6(a - x - y)c$$

which on integration gives, when $x + y = z$ and $k_5b + k_6x = p$,

$$t = \frac{2{\cdot}303}{p - ak_5} \log \frac{a(p - k_5z)}{p(a - z)}$$

Since z is the acid consumed, it can be determined and we have therefore an expression which should yield values of k_6, provided that the values of k_5 previously determined (Fig. 1) can be applied. The constancy of k_6 will be a test of the mechanism.

In practice, the solution of this equation was somewhat difficult and we therefore adopted the following rather laborious procedure. The equation was rearranged to

$$\frac{k_6c + k_5(b - a)}{2{\cdot}303}\, t = \log \frac{a}{k_6c + k_5b} \cdot \frac{k_6c + k_5(b - z)}{a - z}$$

and the known values of k_5, a, b, and c were substituted. Then for each experimental value of z and t a series of arbitrary values of k_6 was introduced and the numerical values of each side of the equation were plotted against k_6. Two curves were thus obtained which at their intersection gave the desired value of k_6.

From the results of the experiments with sodium iodide–hydrogen iodide systems, it would appear that k_5 should be assigned a value corresponding to the equivalent chloride-ion concentration (hydrogen chloride plus lithium chloride) rather than to the hydrogen chloride concentration. However, as was pointed out earlier, the increase in rate with increasing hydrogen chloride occurs to a large extent in the region where ionic dissociation should be small, and where the chlorohydrin in the reaction product is still increasing. Accordingly, the data were calculated for both possible values of k_5. It was found that the value of k_5 obtained at equivalent chloride-ion concentration gave values of k_6 which increased steadily throughout the individual runs, whereas the value of k_5 obtained at equivalent hydrogen chloride concentration gave values of k_6 which were not only constant between runs but were reasonably constant throughout the individual runs, from 20% to 70% conversion.

The range of concentrations over which the equation can be tested is rather limited for a number of reasons. First, the presence of lithium chloride makes difficult the removal of the last traces of pyridine, with the result that the end-point for the acid–base titration is less sharp and very low concentrations cannot be examined. For the same reason the silver nitrate titrations lead to somewhat low values for the percentage of chlorohydrin in the reaction product; it appears that, in general, the proportion of chlorohydrin formed is not greatly changed by the addition of lithium chloride. Secondly, the low value of k_6 relative to k_5 makes necessary a high ratio of lithium chloride to hydrogen chloride in order that the lithium contribution to the overall rate may be determined with some degree of accuracy. Other restrictions are imposed by the form of the integrated equation above. Within these limits, the reaction has been examined with the results shown in Table 4.

TABLE 4.*

HCl	LiCl	Oxide	10^3k_5	10^3k_6	HCl	LiCl	Oxide	10^3k_5	10^3k_6
0·00624	0·0218	0·01715	11·3	1·42	0·01345	0·0613	0·0470	11·6	1·46
0·00624	0·0218	0·0308	11·3	1·42	0·01345	0·0613	0·0346	11·6	1·44
0·00876	0·1046	0·0320	11·4	1·45	0·0210	0·0382	0·0352	11·75	1·30
0·00876	0·0523	0·0323	11·4	1·37	0·0210	0·0382	0·0450	11·75	1·25
0·00876	0·0261	0·0294	11·4	1·44	0·0210	0·0546	0·0335	11·75	1·41
0·00876	0·0105	0·0326	11·4	1·20 [a]	0·0210	0·0546	0·0439	11·75	1·39
0·00957	0·0335	0·0532	11·5	1·50	0·0222	0·0669	0·0387	11·8	1·44
0·00957	0·0335	0·0401	11·5	1·52	0·0222	0·0669	0·0337	11·8	1·40
0·0105	0·0942	0·0314	11·5	1·47	0·0353	0·0623	0·0502	12·0	1·43 [b]
0·0105	0·0471	0·0310	11·5	1·42	0·0353	0·0468	0·0507	12·0	1·30

* Concentrations in moles/l.; k_5 and k_6 in l. mole^{-1} min.$^{-1}$. Chlorohydrin (%) : (*a*) 57; (*b*) 60.

It is evident from the data of Table 4 that, within the limits of concentration reported here, the reaction rate seems to be expressed reasonably well by the expression

$$\mathrm{d[product]/d}t = k_5\mathrm{[oxide][HCl]} + 1{\cdot}4 \times 10^{-3}\mathrm{[oxide][LiCl]}$$

when k_5 is assigned a value obtained from Fig. 1 at equivalent hydrogen chloride concentration. It should be noted, however, that the integrated rate expression is not sufficiently sensitive to small fluctuations in k_6 to permit any very definite conclusions. In practice, excellent results are obtained when the initial mol.-ratio of lithium chloride to hydrogen chloride is at least three to one, since under these conditions k_6 makes an appreciable contribution to the overall rate, particularly in the advanced stages of the reaction. However, with low lithium chloride/hydrogen chloride ratios the value of k_6 in the initial stages of the reaction is usually low and rises steadily as the reaction proceeds. The following typical values of 10^3k_6 illustrate this point (concentrations are given in moles/l.) :

			Reaction, %			
HCl	LiCl	Oxide	15 min.	25 min.	45 min.	55 min.
0·00624	0·0218	0·01715	1·35	1·46	1·40	1·46
0·0203	0·0382	0·0450	1·08	1·18	1·37	1·38

The low values are always obtained under conditions which lead to the greatest experimental error and it is therefore not possible to assess their significance.

The foregoing data, then, seem to indicate that lithium salts, like acids, will promote the reaction of ethylene oxide with pyridine. Qualitative support for this view is obtained from the observation that pyridine solutions of ethylene oxides rapidly turn brown on addition of lithium perchlorate, owing in all probability to the formation of degradation products of 2′-hydroxyethylpyridinium hydroxide. The instability of these pyridinium bases will probably prevent a study of catalysis by lithium salts alone in pyridine solutions, but it may be possible to demonstrate such catalysis in solutions of primary or secondary amines where the reaction involves a simple proton transfer and not proton consumption.

APPLIED CHEMISTRY DIVISION, NATIONAL RESEARCH COUNCIL,
OTTAWA, CANADA.
[*Received, September 24th,* 1951.]