104. *The Mechanism of Epoxide Reactions. Part VII.*[1] *The Reactions of* 1,2-*Epoxybutane,* 3,4-*Epoxybut*-1-*ene,* 1,2-*Epoxy*-3-*chloropropane, and* 1,2-*Epoxy*-3-*methoxypropane with Chloride Ion in Water under Neutral and Acidic Conditions.*

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Rate constants, corrected for the competing hydrolysis, have been determined for the reactions of 1,2-epoxybutane, 3,4-epoxybut-1-ene, 1,2-epoxy-3-chloropropane, and 1,2-epoxy-3-methoxypropane with chloride ion in 9 : 1 v/v water–dioxan at 40°, and at four pH values. The proportions of the isomeric chloro-alcohols in the products, determined by gas chromatography, have been combined with the kinetic results to give rate constants for attack at the normal and at the abnormal positions for both the acid-catalysed and the uncatalysed reactions. Under neutral conditions, electron-withdrawing substituents accelerate the normal and retard the abnormal reaction, as expected. Both the acid-catalysed reactions are retarded by electron-withdrawing substituents and this is explained in terms of the preliminary equilibrium between the epoxide and its conjugate acid.

KINETIC investigations of the polar effects of substituents on the ring opening of epoxides under neutral conditions have previously been carried out [1-3] and the pattern of such effects has been well characterised. The acid-catalysed reaction of 1,2-epoxypropane with

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[1] Part VI, Laird and Parker, *J.*, 1963, 6065.

[2] Addy, Laird, and Parker, *J.*, 1961, 1708.

[3] Laird and Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 4277.

chloride ion has also been studied kinetically and the results have been interpreted in terms of a " borderline " $A2$ mechanism.[4] The effects of substituents on both uncatalysed and acid-catalysed reactions, however, have been studied together on only one occasion,[5] and the normal and abnormal reactions were not distinguished. Thus, while the effects of substituents on the uncatalysed reactions are such as to support an S_N2 mechanism, the effects on the acid-catalysed reactions have not been established.

We have accordingly measured the rates and isomer ratios for the reactions of a series of monosubstituted ethylene oxides with chloride ion in 9 : 1 v/v water–dioxan at 40° and at four pH values. The reactions were followed by continuous titration of the resulting alkali with perchloric acid to maintain the pH constant at the required level. The glycols arising from a competing reaction with water were estimated by periodate titration in duplicate runs, and the rate constants for reaction with chloride ion were corrected for this hydrolysis. Products were analysed by gas chromatography and the individual rate constants were calculated as before.[4] The results are collected in Table 1.

TABLE 1.

Measured rate constants, proportions of normal and abnormal isomers, and rate constants for normal and abnormal attack for the reactions of substituted ethylene oxides with chloride ion at 40° (k_2, k_N, and k_A in l. mole^{-1} sec.$^{-1}$).

Substituent	pH	10^5k_2	Normal product (%)	Abnormal product (%)	10^5k_N	10^5k_A
Chloromethyl	7·0	6·30	100	0	6·30	$<$0·13
	4·5	6·55	100	0	6·55	$<$0·13
	3·8	7·62	100	0	7·62	$<$0·15
	3·6	8·00	100	0	8·00	$<$0·16
Methoxymethyl	7·0	1·80	100	0	1·80	$<$0·04
	4·5	2·18	100	0	2·18	$<$0·04
	3·8	3·22	100	0	3·22	$<$0·06
	3·6	4·00	100	0	4·00	$<$0·08
Ethyl	7·0	1·44	84	16	1·21	0·23
	4·5	3·12	77	23	2·40	0·72
	3·8	10·9	69	31	7·5	3·4
	3·6	15·4	68	32	10·5	4·9
Vinyl	7·0	3·8	14	86	0·5	3·3

Control experiments showed that the gas chromatographic analysis was capable of detecting less than 2% of a minor product isomer and maximum values have accordingly been set for the abnormal rate constants in those reactions where no abnormal isomer was detected (Table 1). Changes in the relative concentrations of the two reactants had no effect on the ratio of isomeric products and the normal and abnormal reactions must therefore be of the same kinetic order. Since the overall reactions obey a second-order rate law at constant pH, the individual reactions must both be of the second order.

Under acidic conditions the observed rates, both for the normal and for the abnormal reactions, represent the sum of the rates of the uncatalysed reaction (rate constant k_W) and of the acid-catalysed reaction (rate constant k_H), and equations (1) and (2) can be applied. Plots of k_N and k_A against the concentration of hydrogen ion gave good straight lines and values of k_W and k_H were obtained from the intercepts and slopes, respectively.

$$k_N = k_{WN} + k_{HN}[H^+] \qquad (1)$$

$$k_A = k_{WA} + k_{HA}[H^+] \qquad (2)$$

All these rate constants are collected in Table 2 and we estimate them to be accurate to ±5%, with the exception of those for the reactions of 3,4-epoxybut-1-ene which are accurate to only about ±20%.

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[4] Addy and Parker, *J.*, 1963, 915.

[5] Brönsted, Kilpatrick, and Kilpatrick, *J. Amer. Chem. Soc.*, 1929, **51**, 428.

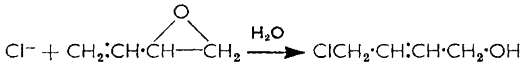
TABLE 2.

Rate constants for the normal and abnormal, catalysed and uncatalysed, attack of chloride ion on substituted ethylene oxides at 40°, together with Taft substituent constants [6,7] (k_{WN} and k_{WA} in l. mole^{-1} sec.$^{-1}$; k_{HN} and k_{HA} in l.^{2} mole^{-2} sec.$^{-1}$).

Substituent	10^5k_{WN}	10^5k_{WA}	10^2k_{HN}	10^2k_{HA}	σ^*	E_s
Chloromethyl	6·30	<0·13	6·8	<0·13	+1·05	−0·24
Methoxymethyl	1·80	<0·04	8·7	<0·17	+0·52	−0·19
Hydrogen [8]	2·05	2·05			+0·49	+1·24
Methyl [4]	1·84	0·30	49·9	31·6	0	0
Ethyl	1·21	0·23	37·4	19·2	−0·10	−0·07
Vinyl †	0·5	3·3			+0·36	−0·07

† Taft substituent constants for vinyl are not available and the values of σ^* and E_s quoted are those for $CH_3{\cdot}CH{=}CH$ and $CH_3{\cdot}CH_2$, respectively.

A rather special situation exists with 3,4-epoxybut-1-ene, where the presence of the double bond in conjugation with the epoxide ring makes possible the formation of a third chloro-alcoholic product, 4-chlorobut-2-en-1-ol, by an S_N2' mechanism:



$$Cl^- + CH_2{:}CH{\cdot}CH{-}CH_2(O) \xrightarrow{H_2O} ClCH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OH$$

This isomer, synthesised by an unambiguous route, was shown to be separable from the other isomers by gas chromatography but no trace of it was found in the reaction product. We estimate that less than 2% could have been detected. The rate measurements for this epoxide are nevertheless subject to considerably greater uncertainty than are those for the other epoxides. A combination of a fast reaction and an unusually high proportion of hydrolysis made the reaction difficult to follow under neutral conditions and impossible under acidic conditions. We believe that the large amount of hydrolysis, especially in acid solution, is attributable to the powerful conjugative electron-release of the vinyl group.

Uncatalysed Reactions.—The results in the second and third columns of Table 2 clearly show that electron-withdrawing groups increase the rate of the normal reaction and decrease that of the abnormal reaction, while electron-releasing groups have the opposite effect. This is in line with the results of a previous investigation of the reactions of a series of *meta*- and *para*-substituted 1,2-epoxyethylbenzenes [3] and it can similarly be explained in terms of a " borderline " S_N2 mechanism, the special geometry of the epoxide ring being responsible for the effect of a polar substituent group operating in opposite directions at the normal and abnormal positions. Application of the Taft equation (3) gives a value $\rho^* = +0{\cdot}52$ (correlation coefficient 0·90, the result for vinyl being excluded)

$$\log k - \log k_0 = \rho^*\sigma^* \qquad (3)$$

for the normal reactions and, although there are insufficient results to enable ρ^* to be evaluated for the abnormal reactions, it is clear that this value is negative.

There is, however, an important difference between the present reactions and those of the 1,2-epoxyethylbenzenes in that the steric effect is kept constant in the latter by the rigidity of the benzene ring and the inclusion of only *meta*- and *para*-substituents. This is not so in the former case and, in order to take proper account of the steric effects, it is desirable to analyse the results in terms of the more complete Taft equation (4),

$$\log k - \log k_0 = \rho^*\sigma^* + \rho_s E_s, \qquad (4)$$

where ρ^* and ρ_s are the reaction constants for the polar and steric effects of substituents, respectively. Application of this equation is possible only for the normal reactions (because of insufficiency of results for the abnormal reactions) and even here the points for vinyl and hydrogen fall well off the line through the points for the other groups. In the case of

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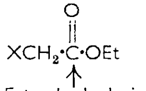
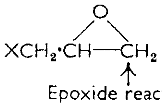
[6] Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 2729, 3120, 5372.
[7] Taft, *J. Amer. Chem. Soc.*, 1953, **75**, 4231, 4534, 4538.
[8] Porret, *Helv. Chim. Acta*, 1944, **27**, 1321.

vinyl this is almost certainly due to the neglect of the resonance effect (see below); in the case of hydrogen it is probably because of the artificially high value for the steric substituent constant of hydrogen (+1·24) given by Taft. The intercept and slope of the best straight line from a plot of $(\log k - \log k_0)/\sigma^*$ against E_s/σ^* give the values $\rho^* = +0{\cdot}71$ and $\rho_s = +1{\cdot}61$ (correlation coefficient 0·99, the results for vinyl and hydrogen being excluded). The value of the polar reaction constant, ρ^*, is not greatly different from that obtained from equation (3) and this seems to indicate that steric effects are not of very great importance in these reactions at the normal position. It is rather surprising to find, therefore, that the steric reaction constant, $\rho_s = 1{\cdot}61$, is appreciably higher than that for ester hydrolysis ($\rho_s = 1{\cdot}00$), especially as the reagents (chloride ion and hydroxide ion) are similar in size and the substituent group is further removed from the point of attack in the epoxides than in the esters:



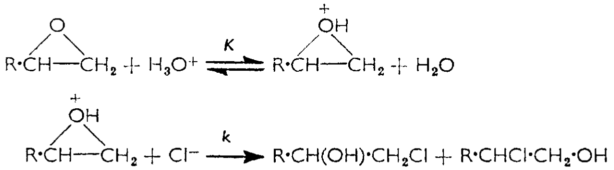
Ester hydrolysis



Epoxide reactions

Whether the rate constants for the normal reactions are analysed by means of equation (3) or equation (4), the point corresponding to 3,4-epoxybut-1-ene falls considerably off the best straight line, the rate constant for the reaction of this compound being substantially less than would be indicated by the line. This is almost certainly due to neglect of the resonance effect of the vinyl group, this electron-releasing conjugative effect more than outweighing the electron-withdrawing polar effect.

Catalysed Reactions.—The results in the fourth and fifth columns of Table 2 indicate that both the normal and the abnormal catalysed reactions have negative polar reaction constants (*i.e.*, the rates of the reactions are increased by electron-releasing groups and decreased by electron-withdrawing groups) and application of equation (3) to the results for the normal reactions confirms this, the best straight line giving a value $\rho^* = -0{\cdot}77$ (correlation coefficient 0·93). In these cases the interpretation of the results is less simple than for the uncatalysed reactions since the rate-determining attack of chloride ion is preceded by an equilibrium between the epoxide and its conjugate acid:



$k_H = Kk$ (5)

Because of the relation expressed in equation (5) the influence of substituent groups on the measured rate constant, k_H, is a resultant of their effect on the equilibrium constant of the first step and on the rate constant of the rate-determining second step. In the first step the epoxide is acting as a base and the effect of substituents will be such as to give a negative reaction constant. In the second step the situation is similar to that for the uncatalysed reactions and we should expect a positive reaction constant for the normal reactions and a negative one for the abnormal reactions. The fact that a negative reaction constant is obtained for both sets of reactions therefore suggests that the (polar) effect of substituents on the initial equilibrium step is dominant over that on the second rate-determining step.

The basicities of the epoxides are not available to provide a quantitative confirmation of this hypothesis, but the abilities of the epoxides to form hydrogen bonds, as measured by their heats of mixing with chloroform,[9] increase in the order: 1,2-epoxy-3-chloropropane < ethylene oxide < 1,2-epoxypropane.

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[9] Searles and Tamres, *J. Amer. Chem. Soc.*, 1951, **73**, 3704; Searles, Tamres, and Lippincott, *ibid.*, 1953, **75**, 2775.

There is no doubt that the reactions are all of the second order at constant pH and, as in the case of 1,2-epoxypropane which we have discussed previously,[4] we believe that the mechanisms for the rate-determining steps of both the normal and abnormal reactions are " borderline " S_N2 (*i.e.*, " borderline " *A*2 for the overall reactions).

EXPERIMENTAL

Materials.—Each of the following four epoxides showed only a single peak when submitted to gas chromatography on a column of diglycerol on Celite.

1,2-*Epoxybutane.* Commercial material (from L. Light and Co., Ltd.) was fractionated through a 60 × 1·5 cm. column packed with Fenske helices, and the middle fraction, b. p. 67°/767 mm. (lit.,[10] 59°), was collected.

1,2-*Epoxy*-3-*chloropropane.* Commercial material (from Mersey Chemicals Ltd.), after repeated fractionation through a column packed with Fenske helices, gave a middle fraction, b. p. 117°/760 mm., n_D^{18} 1·4383 (lit.,[11] 115—116°, n_D^{20} 1·438).

1,2-*Epoxy*-3-*methoxypropane.* Preparation from 1-chloro-3-methoxypropan-2-ol by the method of Flores-Gillardo and Pollard [12] and subsequent fractionation gave a middle fraction, b. p. 111·5°/752 mm. (lit.,[12] 53·5—53·7°/85 mm.).

3,4-*Epoxybut*-1-*ene.* The material prepared from 1-chlorobut-3-en-2-ol by Kadesh's method [13] was distilled through a spinning-band column and gave a middle fraction, b. p. 65—67°/762 mm. (lit.,[13] 65·0—65·8°/739 mm.).

Dioxan. AnalaR dioxan was used without further purification.

Buffer solutions and indicators. These were prepared as described previously.[4]

Rate Measurements.—Rate measurements were carried out as before.[4]

Analysis of Products.—This also was carried out as before,[4] except with 3,4-epoxybut-1-ene. Reaction of this epoxide can give rise to three possible isomers: 1-chlorobut-3-en-2-ol, 2-chlorobut-3-en-1-ol, and 4-chlorobut-2-en-1-ol; and, of these, the last two are not separated by gas chromatography on a column of diglycerol on Celite. Separation of these two isomers is, however, achieved on a column of silicone resin on Celite and a column of this kind was used to demonstrate the absence of 4-chlorobut-2-en-1-ol in the product.

Synthesis of Products.—1-*Chlorobutan*-2-*ol.* Chloroacetaldehyde in ether was added to ethylmagnesium bromide, and the product was hydrolysed [14] to give 1-chlorobutan-2-ol, b. p. 38—39°/9 mm. (lit.,[14] 52°/15 mm.).

2-*Chlorobutan*-1-*ol.* α-Chlorobutyryl chloride, prepared from α-chlorobutyric acid and benzoyl chloride by Brown's method [15] for α-chloropropionyl chloride, was reduced with lithium aluminium hydride to 2-chlorobutan-1-ol, b. p. 48—49°/12 mm. (lit.,[16] 49—53°/13 mm.).

1,3-*Dichloropropan*-2-*ol and* 2,3-*dichloropropan*-1-*ol.* Commercial materials (from Eastman Kodak, Ltd.) were fractionated and the middle fractions collected, b. p. 80—82°/26 mm. (lit.,[17] 174—175°) and 90—92°/29 mm. (lit.,[18] 81·0—81·5°/13·5 mm.), respectively.

1-*Chloro*-3-*methoxypropan*-2-*ol.* 1,2-Epoxy-3-chloropropane was added to a mixture of methanol and concentrated sulphuric acid under reflux [12] and, after neutralisation of the excess of acid with barium carbonate, the filtrate was distilled to give 1-chloro-3-methoxypropan-2-ol, b. p. 66°/11 mm. (lit.,[12] 66°/11 mm.).

2-*Chloro*-3-*methoxypropan*-1-*ol.* Attempts to synthesise this isomer by an unambiguous route were unsuccessful, but it is extremely unlikely that, if it were formed in the reaction of 1,2-epoxy-3-methoxypropane, its presence would fail to be revealed by gas chromatography on a column of diglycerol on Celite.
in tetrahydrofuran [19] and the product was hydrolysed to give 1-chlorobut-3-en-2-ol, b. p. 52°/18 mm. (lit.,[13] 64—65°/30 mm.).

1-*Chlorobut*-3-*en*-2-*ol.* Chloroacetaldehyde in ether was added to vinylmagnesium bromide

[10] Montmollin and Matile, *Helv. Chim. Acta*, 1924, **7**, 106.
[11] Fairbourne, Gibson, and Stephens, *J.*, 1932, 1968.
[12] Flores-Gillardo and Pollard, *J. Org. Chem.*, 1947, **12**, 831.
[13] Kadesh, *J. Amer. Chem. Soc.*, 1946, **68**, 41.
[14] Helfereich and Speidel, *Ber.*, 1921, **54**, 2634.
[15] Brown, *J. Amer. Chem. Soc.*, 1938, **60**, 1325.
[16] Cristol and Eiler, *J. Amer. Chem. Soc.*, 1950, **72**, 4353.
[17] Fairbourne, *J.*, 1930, 381.
[18] Read and Hurst, *J.*, 1922, 996.
[19] Seyferth, *Org. Synth.*, 1959, **39**, 10.

2-*Chlorobut*-3-*en*-1-*ol*. 3,4-Epoxybut-1-ene was added to cooled concentrated hydrochloric acid,[13] and the solution extracted with ether. Distillation of the extract gave 2-chlorobut-3-en-1-ol, b. p. 53°/15 mm. (lit.,[13] 69·5—70°/30 mm.). Although this is not an unambiguous synthesis the product gave a gas chromatogram containing only one peak and was shown to be distinguishable from its two isomers by gas chromatography on either diglycerol or silicone resin.

4-*Chlorobut*-2-*en*-1-*ol*. But-2-ene-1,4-diol was treated with a 0·5 mol. proportion of thionyl chloride in the presence of pyridine.[20] After hydrolysis the solution was extracted with ether and the extract distilled to give 4-chlorobut-2-en-1-ol, b. p. 82—83°/14 mm. (lit.,[20] 79—81°/11 mm.).

All the above products were chromatographically pure when examined on a column of diglycerol on Celite.

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[20] Colonge and Poilane, *Bull. Soc. chim. France*, 1955, 953.