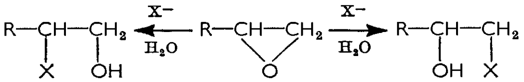
887. *The Mechanism of Epoxide Reactions. Part IX.*[1] *The Reactions of* 1,2-*Epoxypropane and* 3-*Chloro*-1,2-*epoxypropane with Anions in Water under Neutral Conditions*

By E. A. S. Cavell, R. E. Parker, and A. W. Scaplehorn

Rates of the reactions of 1,2-epoxypropane and 3-chloro-1,2-epoxypropane with azide ion in 9 : 1 v/v water–dioxan under neutral conditions have been determined at three temperatures, and Arrhenius parameters evaluated. Some rate measurements have also been made on the reactions of 1,2-epoxypropane with bromide and thiocyanate ions. The kinetic results obtained with azide ion have been shown to conform quite closely to those expected from the literature value of the nucleophilic constant of this reagent. In all the reactions studied, the normal isomer was the principal product obtained.

Ring-opening of monoalkyl-substituted ethylene oxides by anionic nucleophiles under neutral or basic conditions usually results in the formation of the normal isomer (I) (corresponding to substitution at the primary carbon atom of the epoxide ring) as the principal product, owing to the sensitivity of such reactions to steric hindrance (primary steric effect). Apparent exceptions to this general rule are found in the reactions of cyanide[2] and acetylide ions[3] (the latter in liquid ammonia) with 1,2-epoxypropane, for which the major products are said to be the corresponding abnormal isomers (II). In both these reagents there is a multiple bond between the atom involved in the attack on the epoxide



(II) (I)

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[1] Part VIII, R. E. Parker and B. W. Rockett, *J.*, 1965, 2569.

[2] H. S. Davis and B. C. Redmon, U.S.P. 2,390,519/1945 (*Chem. Abs.*, 1946, **40**, 1870).

[3] Thüringische Zellwolle, Belgian P. 448,689/1943 (*Chem. Abs.*, 1947, **41**, 6576).

ring and its nearest neighbour and it is conceivable, therefore, that the anomalous behaviour observed with cyanide and acetylide ions in their epoxide ring-opening reactions is associated with this particular structural feature.[4]

It was with the object of investigating this possibility that the present investigation, a kinetic study of the reactions of azide ion with 1,2-epoxypropane and 3-chloro-1,2-epoxypropane, was undertaken. Azide ion is known to give mainly the abnormal product with (epoxyethyl)benzene, although other small anionic nucleophiles (*e.g.*, methoxide ion) produce major amounts of the normal product as well.[5,6] Rates of ring-opening of 1,2-epoxypropane by bromide and thiocyanate ions have also been measured in order to provide a basis for comparing the rate constant of the ring-opening reaction with the nucleophilicity of the anionic reagent concerned.

EXPERIMENTAL

Materials. Reagent-grade 1,2-epoxypropane and 3-chloro-1,2-epoxypropane were purified by fractional distillation as described previously.[7,8] Sodium azide and sodium bromide were dried before use by heating *in vacuo*. Aqueous solutions of AnalaR potassium thiocyanate were estimated by titration with standard silver nitrate. Dioxan used as solvent for the epoxides in kinetic studies was purified as described previously.[9]

Rate measurements. The kinetic procedure adopted was essentially that described in Part V,[7] stock solutions of the epoxide being prepared in dioxan and of the inorganic salt in water. The neutrality of the reaction mixture (9 : 1 v/v water–dioxan) was maintained by the continuous addition of 72% perchloric acid from a microburette using Bromothymol Blue as indicator, the rate of addition of acid being equivalent to the rate of the epoxide ring-opening reaction. Glycols formed as by-products by hydrolysis of the epoxides were found in no case to exceed 1% of the total reaction product.

Analysis of products. Reaction products, together with unreacted epoxide, were extracted from the reaction mixture with ether after the completion of a kinetic run. The ethereal extract was dried, most of the solvent removed, and the residue examined by vapour-phase chromatography as described previously.[7,8] However, in the present investigation, calibration against synthetic mixtures of known composition was not used because attempts to isolate pure specimens of both isomeric products from the reaction of azide ion with 1,2-epoxypropane were unsuccessful. 1,2-Epoxypropane reacts with sodium azide to give almost entirely one product and both 1-chloropropan-2-ol and 2-chloropropan-1-ol give this same product with sodium azide. The reactions of the two chloro-alcohols evidently proceed by way of ring-closure to the epoxide before the introduction of the azido-group.

Product ratios were therefore estimated from peak areas of the gas chromatograms, these being evaluated both by triangulation and by weighing. This procedure has been found to give satisfactory results in the case of isomeric chloro-propanols and other chloro-alcohols,[7,8] and, by analogy with those cases, it was assumed that here also the less strongly adsorbed product was the normal isomer. This was verified for the azidopropanols as detailed below.

Identification of 1-*azidopropan*-2-*ol*. The product isolated from the appropriate reaction mixture of 1,2-epoxypropane and sodium azide by means of a preparative gas-chromatographic apparatus was found to give only one peak in an analytical gas-chromatographic instrument, and its infrared spectrum had strong absorptions characteristic of the azido-group (2100 cm.$^{-1}$) and the hydroxyl group. It had n_D^{18} 1·4552.[5] Subsequent reduction of this azido-alcohol gave an amino-alcohol which had an infrared absorption spectrum and gas-chromatographic retention time significantly different from those of a specimen of 2-aminopropan-1-ol prepared by the reduction of 2-nitropropan-1-ol with hydrogen gas and Raney nickel. 2-Nitropropan-1-ol was prepared by the condensation of nitro-ethane with formaldehyde.[10]

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[4] R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 756.

[5] C. A. VanderWerf, R. Y. Heisler, and W. E. McEwen, *J. Amer. Chem. Soc.*, 1954, **76**, 1231.

[6] W. Reeve and I. Christoffel, *J. Amer. Chem. Soc.*, 1950, **72**, 1480.

[7] J. K. Addy and R. E. Parker, *J.*, 1963, 915.

[8] J. K. Addy and R. E. Parker, *J.*, 1965, 644.

[9] E. A. S. Cavell, N. B. Chapman, and M. D. Johnson, *J.*, 1960, 1413.

[10] B. M. Vanderbilt and H. B. Hass, *Ind. Eng. Chem.*, 1940, **32**, 34.

RESULTS

Specific rate constants (k_2) for the overall ring-opening reactions were evaluated from the experimental measurements by means of the usual integrated second-order expression and are summarised in Table 1. These rate constants represent the sum of the rate constants for the normal and abnormal reactions, *i.e.*, k_N and k_A, respectively. In the case of the ring-opening reactions of 3-chloro-1,2-epoxypropane, the normal isomer is known to be the only product formed,[5] so that for the reactions of this epoxide k_N and k_2 are identical.

TABLE 1

Measured rate constants, proportions of normal isomers, and rate constants for normal attack (k_2 and k_N in l. mole^{-1}sec.$^{-1}$)

Temp.	Reagent	10^5k_2	Normal product (%)	10^5k_N	Temp.	Reagent	10^5k_2	Normal product (%)	10^5k_N
	(*a*) 1,2-Epoxypropane					(*b*) 3-Chloro-1,2-epoxypropane			
19·7°	N_3^-	6·20	94	5·84	20·0°	N_3^-	23·6	100	23·6
30·0	N_3^-	17·0	92	15·6	30·0	N_3^-	55·0	100	55·0
40·0	N_3^-	42·0	89	37·5	40·0	N_3^-	129	100	129
19·9	Br^-	1·31	*ca.* 95	1·25					
40·0	Br^-	10·1	*ca.* 95	9·6					
19·7	SCN^-	12·4	*ca.* 95	11·8					

TABLE 2

Arrhenius parameters and entropies of activation for the normal reactions (A in l.mole^{-1}sec.$^{-1}$, E in kcal.mole^{-1}, $\Delta S^\ddagger$ in cal.mole^{-1}deg.$^{-1}$)

	$\log A$	E	$\Delta S^\ddagger$ (40°)
3-Chloro-1,2-epoxypropane + azide ion	7·9	15·5	−24·5
1,2-Epoxypropane + azide ion	8·2	16·7	−23·1
1,2-Epoxypropane + bromide ion	8·9	18·5	−19·9
1,2-Epoxypropane + chloride ion [7]	8·4	18·8	−22·2

For the other reactions studied here, product analysis by gas chromatography showed that some of the corresponding abnormal isomer (more strongly adsorbed product) was also formed, although in relatively very small amount so that its exact proportion must be subject to considerable uncertainty. This is especially true in the case of the reactions involving bromide and thiocyanate ions, for which an estimated average value of approximately 95% of normal isomer has been quoted in Table 1. Under the circumstances, evaluation of rate constants for the abnormal reactions is not considered to be justified. The rate constants for the normal reactions are subject to much less uncertainty and their values are given in Table 1.

For comparison with the kinetic data of related reactions,[7] Arrhenius parameters and entropies of activation have been calculated for those normal reactions for which the appropriate rate constants are available, and these are collected in Table 2.

DISCUSSION

Swain and Scott [11] have shown that for a number of nucleophilic reactions it is possible to correlate the relative rates by means of the two-parameter equation (1), in which $k°$ is the rate constant for the reaction of a given substrate with water as reagent and k is the

$$\log k/k° = ns \qquad (1)$$

rate constant for the reaction of the same substrate with any other nucleophile. The substrate constant s is characteristic of the substrate alone and is defined as 1·00 for the reactions of methyl bromide in water at 25°. The nucleophilic constant n is characteristic of the reagent alone and becomes zero when this is water. Both s and n would be expected to depend on temperature and solvent, but Swain and Scott state that, in practice, the variation of s is small for the range from pure water to a solvent mixture containing 50% of water and from 25 to 50°. By implication these approximations apply to n also.

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[11] C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 141.

The kinetic results obtained in the present investigation conform quite closely to equation (1), as shown in Figure 1 in which the values of log k_N for the reactions of 1,2-epoxypropane at 20° have been plotted against the nucleophilic constants of the reagents concerned (the rate constant for the reaction with chloride ion being taken from Part V [7]). A similar plot for the reactions of 3-chloro-1,2-epoxypropane is shown in Figure 2. With the exception of the rate constant for the reaction with azide ion the results used to construct this plot are taken from the work of Brönsted, Kilpatrick, and Kilpatrick [12] and in these reactions the 3-chloro-1,2-epoxypropane is assumed to suffer exculsively normal attack. Measurement of the slopes of the two lines gives values of *s* of 1·00 and 0·96 for the reactions of 1,2-epoxypropane and 3-chloro-1,2-epoxypropane, respectively. These values are very similar to that for the reactions of methyl bromide (1·00) and this is not entirely consistent with other evidence that leads to the conclusion that epoxide ring-opening reactions are of the type of bimolecular reactions in which bond-breaking is dominant.[4,7] Inconsistencies of this kind have been pointed out before in the Swain and Scott treatment.[13]

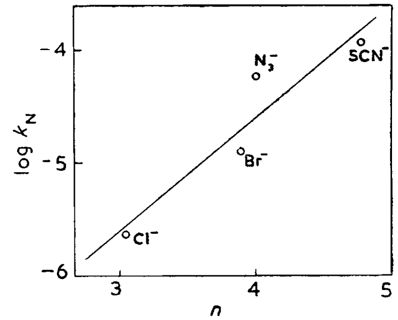

FIGURE 1. Plot of log k_N against nucleophilic constant *n* for reactions of 1,2-epoxypropane

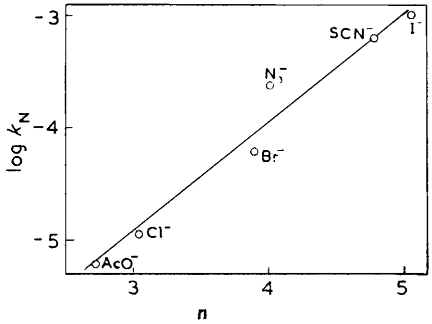

FIGURE 2. Plot of log k_N against nucleophilic constant *n* for reactions of 3-chloro-1,2-epoxypropane

No great significance can be attached to the apparently higher-than-expected reactivity of the azide ion (Figures 1 and 2), because Swain and Scott's value of the nucleophilic constant for this reagent is dependent on one reaction only. Furthermore, the isomer ratios and Arrhenius parameters for the reactions of azide ion studied here show no marked differences from those for the reactions of the other nucleophiles. In these circumstances the preponderance of abnormal isomer in the reactions with cyanide and acetylide ions cannot be attributed to the presence of multiple bonds in these reagents, and the explanation probably lies in the particular reaction conditions used. In the cyanide reactions,[2] for example, equivalent amounts of hydrogen cyanide and epoxide were heated together under pressure to above 90° and, although the effective nucleophile is undoubtedly cyanide ion, the presence of acid (HCN) and the use of a high temperature are both known to favour abnormal attack.[7]

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[12] J. N. Brönsted, M. Kilpatrick, and M. Kilpatrick, *J. Amer. Chem. Soc.*, 1929, **51**, 428.

[13] E. S. Gould, " Mechanism and Structure in Organic Chemistry," Holt, Rinehart, and Winston, New York, 1959, p. 301.