

## Kinetics of Formation of Substituted Styrene Oxides by Reaction of 2-Aryl- and 1-Aryl-2-halogenoethanols with Aqueous Alkali

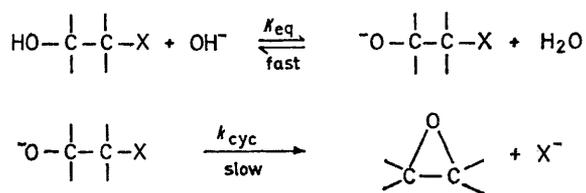
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The kinetics of formation of *m*- and *p*-substituted styrene oxides by reaction of 1- and 2-aryl-2-halogenoethanols with aqueous alkali have been interpreted according to the Winstein–Lucas mechanism. The respective Hammett  $\rho$  values for overall reaction of 1- and 2-aryl-2-halogenoethanols are 0.32 and -1.13. The effects of substituents on the pre-equilibria have been estimated and it is concluded that the  $\rho$  values for the respective cyclizations are -0.34 and -1.61. The relative rates of dehalogenation of 2-halogeno-2-phenylethanols ( $k_{Cl}:k_{Br}:k_{I} = 0.035:1.3:1$ ) have been contrasted with those for other systems. The effect of phenyl substitution on the rate of formation of three-membered rings is discussed.

CYCLODEHYDROHALOGENATION of  $\beta$ -halogenoalcohols has been widely used to produce epoxides, and evidence for a mechanism involving cyclization of an intermediate alkoxide anion has been contributed by many workers.<sup>1</sup>

Investigation has been made of the effect of alkyl<sup>2-4</sup> and vinyl<sup>5</sup> substitution on the rate of epoxide formation and cyclization kinetics of alkyl and phenyl substituted chlorohydrins along with those of *cis*- and *trans*-2-chlorocyclohexanol have been reported.<sup>6</sup>

Four papers have dealt with the rate of cyclization of styrene halogenohydrins although only the  $\beta$ -halogeno-compounds were studied.<sup>6-9</sup> In all cases the mechanism of formation of epoxides from halogenohydrins proposed by Winstein and Lucas<sup>10</sup> has been assumed (Scheme).



SCHEME

The experimental velocity constant may be defined by equation (1) where  $d[\text{X}^-]/dt = k_{\text{exp}} [\text{Halogenohydrin}]$

$$k_{\text{exp}} = k_{\text{cyc}} K_{\text{eq}} \quad (1)$$

$[\text{OH}^-]$ .  $k_{\text{exp}}$  is a second-order constant and  $K_{\text{eq}} = K_a/K_w$  where  $K_a$  is the acid dissociation constant of the halogenohydrin and  $K_w$  is the ionic product of water.

Bergkvist<sup>6</sup> measured the rate of reaction of styrene  $\beta$ -bromohydrin in sodium carbonate–hydrogen carbonate buffer at 25°. Barantsevich and Temnikova<sup>8</sup> repeated the investigation and followed the reaction of the  $\beta$ -chlorohydrin by both a potentiometric and a conducto-

metric method. An inverse relationship was found between  $k_{\text{exp}}$  and the dielectric constant of the solvent for a limited range of dioxan–water mixtures. This was analogous to the trend reported by Stevens *et al.*<sup>11</sup> who studied the cyclization of ethylene chlorohydrin. Comprehensive studies of the effect of alcoholic solvents on the equilibrium and cyclization steps of the reaction of ethylene chlorohydrin have been reported<sup>11-13</sup> and the effect of change in dielectric constant is primarily on the later step.

The effect of aryl substituents on the rate of styrene oxide formation from the corresponding  $\beta$ -chlorohydrins was subsequently determined. The activation parameters and cyclization rate constants were compared with those for aliphatic chlorohydrins  $\text{R}^1\text{R}^2\text{C}(\text{OH})\text{CH}_2\text{Cl}$  ( $\text{R}^1 = \text{R}^2 = \text{H}$ ;  $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{Me}$ ;  $\text{R}^1 = \text{R}^2 = \text{Me}$ ; and  $\text{R}^1 = \text{R}^2 = \text{Et}$ ). It was considered that the effect of substituents on acidity of the alcohol mainly accounted for the positive  $\rho$  value for the former series and that the contrary result for formation of alkyl substituted ethylene oxides was in agreement with Streitwieser's hypothesis that a neighbouring alkyl group accelerates three-membered ring formation.<sup>14</sup>

Rates of formation of styrene oxide by reaction of  $\beta$ -halogenophenethyl alcohols in aqueous base have not been reported, nor has the effect of ring substituents been determined. This study was undertaken with the expectation that marked anchimeric assistance of halide ion release, by neighbouring alkoxide, would be a feature of this system. It was of interest to determine and contrast the rate of dehalogenation and influence of *m*- and *p*-substituents with results for closely related systems in which neighbouring charged groups (*e.g.*  $\text{CO}_2^-$ ) are believed to act electrostatically without bond formation in the rate-determining step.<sup>15</sup>

<sup>1</sup> A. Rosowsky in 'Heterocyclic Compounds with Three- and Four-membered Rings,' ed. A. Weissberger, Interscience, New York, 1964, Part I, (a) p. 1; (b) p. 94; (c) p. 95; (d) p. 270.

<sup>2</sup> H. Nilsson and L. Smith, *Z. phys. Chem.*, 1933, **166A**, 136.

<sup>3</sup> G. Forsberg, *Acta Chem. Scand.*, 1954, **8**, 135.

<sup>4</sup> P. Croisier and P. J. L. Fierens, *Bull. Soc. chim. belges*, 1956, **65**, 207.

<sup>5</sup> R. G. Kadesch, *J. Amer. Chem. Soc.*, 1946, **68**, 46.

<sup>6</sup> T. Bergkvist, *Svensk kem. Tidsskr.*, 1947, **59**, 224 (*Chem. Abs.*, 1948, **42**, 5317f).

<sup>7</sup> T. Bergkvist, *Svensk kem. Tidsskr.*, 1947, **59**, 194 (*Chem. Abs.*, 1948, **42**, 5317i).

<sup>8</sup> E. N. Barantsevich and T. I. Temnikova, *Zhur. org. Khim.*, 1966, **2**, 648 (*Chem. Abs.*, 1966, **65**, 8800g).

<sup>9</sup> E. N. Barantsevich and T. I. Temnikova, *Reakts. spos. org. Soedinenii, Tartu. Gos. Univ.*, 1966, **3**, 81 (*Chem. Abs.*, 1967, **66**, 115,200v).

<sup>10</sup> S. Winstein and H. J. Lucas, *J. Amer. Chem. Soc.*, 1939, **61**, 1576.

<sup>11</sup> E. Stevens, C. McCabe, and I. Warner, *J. Amer. Chem. Soc.*, 1948, **70**, 2449.

<sup>12</sup> C. McCabe and J. L. Warner, *J. Amer. Chem. Soc.*, 1948, **70**, 4031 and earlier papers cited therein.

<sup>13</sup> L. Winstrom and I. Warner, *J. Amer. Chem. Soc.*, 1939, **61**, 1205.

<sup>14</sup> A. Streitwieser, 'Solvolytic Displacement Reactions,' McGraw-Hill, New York, 1962 (a) p. 111; (b) pp. 112, 124.

<sup>15</sup> F. G. Bordwell and A. C. Knipe, *J. Org. Chem.*, 1970, **35**, 2959.

## RESULTS AND DISCUSSION

Reactions of  $\beta$ -chlorophenethyl alcohol and its *m*-methyl, *p*-chloro-, *m*-methoxy-, *m*-nitro-, and *p*-nitro-derivatives in aqueous sodium hydroxide have been studied at 25°. The influence of substituents has been evaluated by means of the Hammett equation. The effect of the leaving group for  $\beta$ -chloro-,  $\beta$ -bromo-, and  $\beta$ -iodo-phenethyl alcohols has been contrasted with related systems. Epoxidations of  $\beta$ -bromo- $\alpha$ -phenylethyl alcohol and its *p*-methyl and *p*-nitro-derivatives have also been studied and the results have been compared with those for  $\alpha$ -aryl- $\beta$ -chloro-alcohols.<sup>6,9</sup>

$\alpha$ - or  $\beta$ -Arylethylhalogeno-alcohols were respectively prepared by reduction of phenacyl halides or by regio-specific ring opening of the appropriate epoxides with the hydrogen halide in dry chloroform at 0°.

Aryl substituted styrene oxides were prepared either by interaction of the corresponding araldehyde with trimethyl sulphonium ylide in dimethyl sulphoxide or by cyclization of a halogenohydrin. The reaction of each compound was followed, as described in the Experimental section, over a 1–2 pH range and the apparent second-order rate constant  $k_{\text{exp}}$  was determined by dividing  $k'$  (the first-order rate constant at constant pH) by the hydroxide concentration. If the Winstein-Lucas mechanism is adopted equations (2)–(4) apply, leading to equations (5) and (6). Values of  $k_{\text{exp}}$  were constant to

$$K_{\text{eq}} = \frac{[\text{ArCHXCH}_2\text{O}^-]}{([\text{ArCHXCH}_2\text{OH}][\text{OH}^-]} \quad (2)$$

$$d[\text{X}^-]/dt = k_{\text{cyc}}[\text{ArCHXCH}_2\text{O}^-] \quad (3)$$

$$= k_{\text{cyc}}K_{\text{eq}}[\text{OH}^-][\text{ArCHXCH}_2\text{OH}] \quad (4)$$

$$k' = k_{\text{cyc}}K_{\text{eq}}[\text{OH}^-] \quad (5)$$

$$k_{\text{exp}} = k_{\text{cyc}}K_{\text{eq}} = k'/[\text{OH}^-] \quad (6)$$

within a few % over as much as a 100-fold change in base concentration and only in the case of  $\beta$ -bromo- and  $\beta$ -iodo-phenethyl alcohol were the kinetics complicated by reaction of the un-ionized alcohols.

The rate of reaction of the undissociated bromo-alcohol ( $k_1 = 5.8 \times 10^{-4} \text{ s}^{-1}$ ) is 966-fold slower than that of  $\alpha$ -phenylethyl bromide under the same conditions ( $k = 0.56 \text{ s}^{-1}$ ). This is consistent with the rate retardation expected of an  $S_{\text{N}}1$  reaction of a tertiary halide (or its equivalent) upon substitution of a  $\beta$ -hydroxy-group.<sup>14b</sup>

In Table 1 are listed the values  $k'$  and  $k_{\text{exp}}$  for reaction of substituted  $\beta$ -chlorophenethyl alcohols at 25° over a range of pH values. Table 2 lists  $k'$  and  $k_{\text{exp}}$  values for the  $\beta$ -chloro-,  $\beta$ -bromo-, and  $\beta$ -iodo-phenethyl alcohols. In Table 3 the mean  $k_{\text{exp}}$  values are listed for all compounds studied (values for the bromo- and iodo-alcohols have been corrected for reaction of the un-ionized alcohol).

The relative rates of reaction ( $k_{\text{exp}}$ ) of  $\beta$ -halogeno- $\beta$ -

† The estimated  $K_{\text{a}}$  values are subject to a probable error in  $\text{p}K_{\text{a}}$  of  $\pm 0.1$  ( $\pm 26\%$  error in  $K_{\text{a}}$ ). The  $K_{\text{a}}$  ratios should however be more reliable than this would suggest since errors which arise through allowance for the influence of halogen or phenyl substituents should have a systematic, rather than random effect throughout the series.

TABLE 1

Rates \* of reaction of  $\beta$ -chlorophenethyl alcohols  $\text{YC}_6\text{H}_4\text{CHClCH}_2\text{OH}$  with aqueous sodium hydroxide at 25 °C

Y	pH	$[\text{YC}_6\text{H}_4\text{CHClCH}_2\text{OH}]_M$	$10^4 k'/\text{s}^{-1}$	$k_{\text{exp}}/1 \text{ mol}^{-1} \text{ s}^{-1}$	Mean $k_{\text{exp}}$
H	9.0	0.0029	3.56	35.6	34.5
	9.0	0.0015	3.76	37.6	
	9.5	0.0015	10.8	34.0	
	10.05	0.0015	38.2	34.0	
	10.4	0.0015	83.6	33.3	
<i>m</i> -Me	9.4	0.0015	10.4	41.4	39.0
	9.6	0.0015	15.1	37.9	
	10.05	0.00075	41.5	37.0	
	10.4	0.00075	99.9	39.8	
<i>p</i> -Cl	9.0	0.0015	3.25	32.5	31.4
	9.4	0.0015	8.03	32.0	
	10.05	0.0015	34.7	30.9	
	10.05	0.00075	35.3	31.5	
	10.4	0.0015	75.7	30.2	
<i>m</i> -MeO	9.0	0.0015	2.42	23.5	23.4
	9.4	0.0015	5.84	23.3	
	10.05	0.0015	24.9	22.2	
	10.4	0.0015	61.8	24.6	
	10.4	0.0029	58.5	23.3	
<i>m</i> -NO <sub>2</sub>	9.42	0.0015	1.36	5.16	5.21
	9.6	0.0015	2.07	5.20	
	10.05	0.0015	6.15	5.48	
	10.4	0.0015	12.9	5.10	
	10.4	0.0029	12.9	5.13	
<i>p</i> -NO <sub>2</sub>	10.05	0.0015	5.46	4.87	4.7
	10.4	0.0015	11.4	4.54	

\* Each rate constant is the average of at least three runs. The correlation coefficient of each first order plot ( $\log [\text{YC}_6\text{H}_4\text{CHClCH}_2\text{OH}]$  versus time) to beyond 85% completion of reaction was better than 0.998.

TABLE 2

Reaction of  $\beta$ -halogenophenethyl alcohols with aqueous sodium hydroxide at 25 °C

PhCHXCH <sub>2</sub> OH	pH	$10^5 k'/\text{s}^{-1}$	$k_{\text{exp}}/1 \text{ mol}^{-1} \text{ s}^{-1}$
X = Cl	9.0	36.6	36.6
	9.5	108	37.6
	10.05	382	34.0
	10.4	836	33.0
X = Br *	5.0	58	580,000
	7.0	71.6	7170
	8.0	162	1620
	8.5	421	1331
X = I *	4.99	9.11	
	5.0	9.83	98,300
	5.83	11.2	16,570
	7.0	20.3	2030
	8.0	93.4	934
	9.0	(1.1–1.3) $\times 10^3$	1100–1300

\*  $k_{\text{exp}}$  Values appear artificially high at low pH because of the contribution by solvolysis of the un-ionized halogeno-alcohols to the rate of halide ion release.

phenylethanols with hydroxide ion have been determined (Cl : Br : I = 0.35 : 1.3 : 1) and follow the trend (0.018 : 1.1 : 1) already reported<sup>12</sup> for formation of ethylene oxides from ethylene halogenohydrins. Using literature values<sup>16,17</sup> one may estimate †  $K_{\text{CH}_2\text{OCH}_2\text{OH}}$

<sup>16</sup> G. B. Barlin and D. D. Perrin, *Quart. Rev.*, 1966, **20**, 75.

<sup>17</sup> P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, 1960, **82**, 795.

$= 3.9 \times 10^{-15}$ ,  $K_{\text{CH}_2\text{BrCH}_2\text{OH}} = 3.3 \times 10^{-15}$ , and  $K_{\text{CH}_2\text{ICH}_2\text{OH}} = 2.0 \times 10^{-15}$ . For the ethylene halogenohydrins the  $K_{\text{eq}}$  ratios (Cl:Br:I) therefore become 1.9:1.6:1 and require that the corresponding values of  $k_{\text{cyc}}$  are in the ratio 0.0094:0.68:1. The values of

TABLE 3

Mean values of  $k_{\text{exp}}$  for reaction of  $\beta$ -halogenophenethyl alcohols in aqueous sodium hydroxide at 25 °C

Y C <sub>6</sub> H <sub>4</sub> CHXCH <sub>2</sub> OH		$k_{\text{exp}}/\text{l mol}^{-1} \text{s}^{-1}$
X	Y	
Cl	H	34.5
Br	H	ca. 1330 * †
I	H	ca. 1000 * ‡
Cl	<i>m</i> -Me	39.0
Cl	<i>p</i> -Cl	31.4
Cl	<i>m</i> -MeO	23.4
Cl	<i>m</i> -NO <sub>2</sub>	5.21
Cl	<i>p</i> -NO <sub>2</sub>	4.70

\* Estimated from the rate of reaction at high base concentration where contribution ( $k_1$ ) from solvolysis of un-ionized alcohol was negligible. †  $k_1$  ca.  $5.8 \times 10^{-4} \text{s}^{-1}$ . ‡  $k_1$  ca.  $1.0 \times 10^{-4} \text{s}^{-1}$ .

the acid dissociation constants for the  $\beta$ -halogenophenethyl alcohols may be estimated<sup>16</sup> if an additional acid strengthening effect of ca. 0.31 p*K*<sub>a</sub> units is attributed to the  $\beta$ -phenyl substituent, and become  $K_{\text{Cl}} = 8.0 \times 10^{-15}$ ,  $K_{\text{Br}} = 6.8 \times 10^{-15}$ , and  $K_{\text{I}} = 4.2 \times 10^{-15}$  respectively. The ratios remain 1.9:1.6:1; therefore the rate constants  $k_{\text{cyc}}$  and hence the leaving group abilities are in the ratio Cl:Br:I = 0.018:0.8:1.

**Hammett Relationships.**—For  $\beta$ -aryl  $\beta$ -chloroethanols a Hammett correlation has been found between the logarithm of the rate constants  $k_{\text{exp}}$  and the substituent constant  $\sigma$ . The  $\rho$  value is  $-1.13$  and correlation coefficient  $r$  0.994. In order to determine the  $\rho$  value for the cyclization step ( $k_{\text{cyc}}$ ) alone it is necessary to allow for the dependence of  $K_{\text{a}}$  on substituents since  $k_{\text{exp}} = K_{\text{a}}k_{\text{cyc}}$ . The acid dissociation constants of the alcohols

TABLE 4

$k_{\text{cyc}}$  For reaction of  $\beta$ -chlorophenethyl alcohols Y C<sub>6</sub>H<sub>4</sub>CHCl-CH<sub>2</sub>OH in aqueous sodium hydroxide at 25 °C, evaluated from  $k_{\text{exp}}$  and estimated\* values of  $K_{\text{a}}$  (p*K*<sub>a</sub> = 14.0 - 0.49 $\sigma$ ,  $k_{\text{cyc}} = k_{\text{exp}}K_{\text{a}}/K_{\text{a}}$ )

Y	$\sigma$	p <i>K</i> <sub>a</sub>	$10^{15}K_{\text{a}}$	$1 \text{ mol}^{-1} \text{s}^{-1}$	$k_{\text{cyc}}/\text{s}^{-1}$
H	0	14.0	10	34.5	34.5
<i>m</i> -Me	-0.069	14.03	9.2	39.0	42.2
<i>p</i> -Cl	+0.227	13.89	12.9	31.4	24.4
<i>m</i> -MeO	+0.115	13.94	11.4	23.4	20.5
<i>m</i> -NO <sub>2</sub>	+0.710	13.65	22.3	5.21	2.34
<i>p</i> -NO <sub>2</sub>	+0.778	13.62	24.0	4.70	1.96

\* The p*K*<sub>a</sub> for  $\beta$ -chlorophenethyl alcohol (14.0) is based on the experimentally determined value<sup>17</sup> for  $\beta$ -chloroethanol (14.31) with a correction<sup>16</sup> ( $-0.31$ ) for the effect of a  $\beta$ -phenyl group.

may be estimated if it is assumed that the influence of *m*- and *p*-aryl substituents parallels their effect on acidity of phenylacetic acids for which  $\rho$  0.49 has been determined.<sup>18</sup> In Table 4 are listed the values  $k_{\text{exp}}$ , p*K*<sub>a</sub>

<sup>18</sup> H. H. Jaffe, *Chem. Rev.*, 1953, **53**, 191.

<sup>19</sup> J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions,' Wiley, New York, 1963, p. 243.

(estimated),  $K_{\text{a}}$ , and  $k_{\text{cyc}}$  (from  $k_{\text{exp}}$  and  $K_{\text{a}}$ ). For the *p*-chloro-substituent,  $\sigma^+$  correlates better than  $\sigma$  for a plot of  $\log k_{\text{cyc}}$  versus Hammett  $\sigma$  values. The fit is excellent ( $r = 0.999$ ) and a relatively large negative  $\rho$  value ( $-1.61$ ) is obtained. This is indicative of a transition state in which C-Cl bond heterolysis is well advanced.

The influence of substituents on the nucleophilicity of the alkoxide ion might also, in part, contribute to the negative  $\rho$  value. In general the rate of attack of a nucleophile on a carbon atom parallels its affinity for protons<sup>19</sup> within narrow structural limits. The rate of nucleophilic substitution may be related to  $K_{\text{a}}$  by an expression which is analogous to the Brønsted relation-

$$\log k_{\text{n}} = \alpha \log K_{\text{b}} + c \quad (7)$$

$$= -\alpha \log K_{\text{a}} + c' \quad (8)$$

ship although the positive value of  $\alpha$  need not be restricted to less than unity. For a series of phenols, benzoic acids, and phenylacetic acids bearing *m*- and *p*-substituents, the acid dissociation constants may be related to the substituent  $\sigma$  values by the expression (9).

$$\log K_{\text{a}} = \log K_{\text{a}}^{\text{H}} + \sigma \rho_{\text{a}} \quad (9)$$

Substitution of equation (9) into (8) gives (10). There-

$$\log k_{\text{n}} = -\alpha \log K_{\text{a}}^{\text{H}} - \alpha \sigma \rho_{\text{a}} + c' \quad (10)$$

fore a plot of  $\log k_{\text{n}}$  versus  $\sigma$  will give a slope  $\rho_{\text{n}} = -\alpha \rho_{\text{a}}$ . Results<sup>18,20</sup> for nucleophilic displacement of substituted phenoxide and benzoate ions suggest that  $\alpha$  is generally positive and less than unity. Thus the variation of the nucleophilicity of the alkoxide ion in the intramolecular epoxidation of  $\beta$ -aryl- $\beta$ -chloroethanols (where  $\log k_{\text{cyc}} =$



$\log k_{\text{cyc}}^{\text{H}} + \sigma \rho_{\text{cyc}}$ ) should be represented by a component ( $\rho_{\text{n}}$ ) of  $\rho_{\text{cyc}}$  no more negative than  $-0.49$  since  $\rho_{\text{a}}$  for the acid dissociation of phenylacetic acids =  $+0.49$  and  $\rho_{\text{n}} = -\alpha \rho_{\text{a}}$ . Therefore of the overall  $\rho$  value ( $\rho_{\text{cyc}} = -1.61$ ) for the cyclization step, more than  $-1.13$  can be attributed to effects other than substituent dependence ( $\rho_{\text{n}}$ ) of the nucleophilicity of the alkoxide ion.

Rates<sup>21</sup> of formation of styrene oxides from styrene  $\beta$ -chlorohydrin and its *p*-methyl and *p*-bromo-derivatives in aqueous hydroxide have been tabulated (Table 5) along with those here reported for styrene  $\beta$ -bromohydrin and its *p*-methyl and *p*-nitro-derivatives. It is evident that electron-withdrawing substituents increase the overall rate of reaction of either the chloro- or bromo-compounds and that the Hammett  $\rho$  value is ca.  $+0.3$  for reaction of these halogenohydrins.

Results of a more detailed study<sup>9</sup> of the epoxidation of *m*- and *p*-substituted  $\beta$ -chloro- $\alpha$ -phenylethyl alcohols have also been analysed. Logarithms of  $k_{\text{exp}}$ ,  $K_{\text{eq}}$ , and

<sup>20</sup> G. F. Smith, *J. Chem. Soc.*, 1943, 521.

<sup>21</sup> T. Bergkvist, *Svensk kem. Tidshkr.*, 1947, **59**, 205.

$k_{\text{cyc}}$  for 25° are related to the corresponding  $\sigma$  values by the  $\rho$  values 0.32, 0.62, and -0.34 respectively.

In this case the influence of substituents on the nucleophilicity of the alkoxide ion will be pronounced although once again it is probable that the nucleophilic component

TABLE 5

Rates of formation of *m*- and *p*-substituted styrene oxides from  $\alpha$ -aryl- $\beta$ -halogenoethanols in aqueous sodium hydroxide at 25 °C

Y	X	$k_{\text{exp}}/\text{l mol}^{-1} \text{s}^{-1}$	$\sigma$	$\rho \dagger$
H	H	0.66 <sup>a</sup>	0	
<i>p</i> -Me	Cl	0.63 <sup>a</sup>	-0.170	0.12
<i>p</i> -Br	Cl	0.85 <sup>a</sup>	+0.232	ca. 0.5
H	Br	30.7 <sup>b</sup>	0	
<i>p</i> -Me	Br	21.6 <sup>b</sup>	-0.170	0.4
<i>p</i> -NO <sub>2</sub>	Br	51.5 <sup>b</sup>	+0.778	0.3

<sup>a</sup> Ref. 21. <sup>b</sup> This work.

$\dagger \rho = \log(k_{\text{Y}}/k_{\text{H}})/\sigma_{\text{Y}}$

( $\rho_{\text{n}}$ ) of the value  $\rho_{\text{cyc}}$  will be given by  $\rho_{\text{n}} = -\alpha\rho_{\text{a}}$  where  $\alpha$  is less than unity and  $\rho_{\text{a}}$  relates the acid dissociation constants. Thus the component of  $\rho$  attributable to aspects of heterocycle formation exclusive of effects on alkoxide nucleophilicity lies between -0.34 and +0.3. This is in contrast to the range -(1.13-1.61) estimated for the  $\beta$ -aryl- $\beta$ -chloroethoxides which almost certainly feature more advanced carbon-chlorine bond cleavage in the transition state.

The similarity between effects of ring substituents on cyclization of  $\beta$ -chloro- $\beta$ -phenylethoxide ion ( $\rho = -1.61$ ) and on 'abnormal' ring opening of styrene oxide by benzylamine<sup>22</sup> ( $\rho = -1.15$ ) is apparent. The transition state for either reaction can be likened to that depicted by Parker and Isaacs<sup>23</sup> for borderline  $S_{\text{N}}2$  reaction of epoxides.

The  $\rho$  value for halide release from  $\beta$ -aryl- $\beta$ -chloroethoxide ions is much less negative than those reported for debromination of the anions of aryl(bromo)acetate,<sup>24,25</sup> 3-aryl-3-bromopropionate,<sup>15</sup> and 3-aryl-2,3-dibromopropionate<sup>15</sup> ( $\rho = -2.94$ ,  $-3.24$ , and  $-3.19$  respectively, in water at 25°). It has been argued that for these systems the neighbouring effect of carboxylate ion is electrostatic or inductive in origin, there being no anchimeric assistance attributable to C-O bond formation. Formation of an intermediate zwitterion by C-X heterolysis is envisaged and, as one would expect, the sensitivity to aryl substituents is almost identical in each case. That the zwitterion mechanism does not apply for reaction of the analogous alkoxides is suggested by the much less negative  $\rho$  value. However, the relative magnitudes of the dehalogenation rate constants (Table 6) provide more striking evidence of the differences between carboxylate and alkoxide systems.

Debromination of  $\alpha$ -phenylethyl bromide is accelerated 4000-fold by the introduction of a  $\beta$ -oxy anion

<sup>22</sup> R. M. Laird and R. E. Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 4277.

<sup>23</sup> R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.

<sup>24</sup> F. G. Bordwell and A. C. Knipe, *J. Org. Chem.*, 1970, **35**, 2956.

TABLE 6

Effect of substituents (R) on rate of halide ion release from PhCHXR in water at 25 °C

PhCHXR	$k/\text{s}^{-1}$	Ref.
PhCHClCH <sub>3</sub>	$4.8 \times 10^{-2}$	26
PhCHClCH <sub>2</sub> O <sup>-</sup>	43.4	
PhCHClCH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> <sup>-</sup>	0.14	27 *
PhCHClCH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> Me	$5.5 \times 10^{-3}$	27
PhCHBrCH <sub>3</sub>	0.56	26
PhCHBrCH <sub>2</sub> O <sup>-</sup>	$1.97 \times 10^3$	
PhCHBrCO <sub>2</sub> <sup>-</sup>	$2.93 \times 10^{-4}$	24
PhCHBrCH <sub>2</sub> CO <sub>2</sub> <sup>-</sup>	0.14	15
PhCHBrCH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> <sup>-</sup>	1.3	27 *

\* By extrapolation of results for 20-80% aqueous EtOH.

whereas bromo(phenyl)acetate and 2-bromo-3-phenylpropionate ions react 200- and 4-fold slower. Recent results have made it clear that anchimeric assistance is not a feature of reaction of 4-bromo-4-phenylbutanoate ion which reacts only three times faster than  $\alpha$ -phenylethyl bromide, even though the anion is in the position generally most favourable for neighbouring-group participation.<sup>28</sup> The effect of aryl substituents on this system are currently being investigated.

*The Effect of Phenyl and Vinyl Substituents on Rate of Formation of Epoxides.*—The relative rates of cyclization of the halogenophenylethoxide and halogenoethoxide ions may be compared. Table 7 lists values of  $k_{\text{cyc}}$  which have been obtained from  $k_{\text{exp}}$  and estimated values of  $K_{\text{a}}$ . Included in Table 7 are the values for reaction of  $\beta$ -halogeno- $\alpha$ -phenylethanol. Experimentally determined  $\text{p}K_{\text{a}}$  values are listed for comparison with those estimated as described. It is clear that an  $\alpha$ -phenyl substituent enhances the rate of cyclization of  $\beta$ -chloro- and  $\beta$ -bromo-ethyl alcohol by 11.7- and 8-fold respectively. For a phenyl group in the  $\beta$ -position the increases are much greater, being 2150-, 1500-, and 1000-fold for the chloride, bromide, and iodide and suggests that there may be considerable carbon-halogen bond heterolysis in the transition state as this is the trend expected of a process with  $S_{\text{N}}1$  rather than  $S_{\text{N}}2$  character. Results for aziridine formation from amino-sulphate ions have been discussed in detail elsewhere<sup>29</sup> and are included for comparison.

The effect on the epoxide ring closure of a phenyl substituent  $\alpha$  to the alkoxide ion, can best be determined by compensation for its effect on the nucleophilicity of the ion. Thus rate enhancement attributable to direct phenyl-epoxide conjugation or interaction could be determined by comparison of the rates of cyclization of  $\beta$ -chloroethoxides of identical  $\text{p}K_{\text{a}}$  (the assumption being that proton affinity and nucleophilicity are almost identically related for the two chlorohydrins). The  $\text{p}K_{\text{a}}$  of styrene chlorohydrin is 13.64 and the  $\rho$  value for this acid dissociation is 0.62. A ring substituent having  $\sigma = -1.08$  will increase the  $\text{p}K_{\text{a}}$  value to 14.31 which is

<sup>25</sup> K. C. Kemp and D. Metzger, *J. Org. Chem.*, 1968, **33**, 4165.

<sup>26</sup> A. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, 1957, **79**, 1597, 1602.

<sup>27</sup> A. C. Knipe, unpublished results.

<sup>28</sup> B. Capon, *Quart. Rev.*, 1964, **18**, 45.

<sup>29</sup> C. S. Dewey and R. A. Bafford, *J. Org. Chem.*, 1967, **32**, 3108.

identical to that for ethylene chlorohydrin. However, if the  $\rho$  value correlating  $k_{\text{cyc}}$  with  $\sigma$  is  $-0.34$  then the rate enhancement due to aryl-epoxide interaction, estimated by comparison of the cyclization rate constants for these two chloroalkoxide ions, becomes 27-fold.

formation of ethylene oxide from halogenohydrins has been reported by McCabe and Warner.<sup>12</sup> The apparently anomalous accelerating effect of lithium or sodium perchlorate on the rates of formation of styrene oxides is being investigated further.

TABLE 7

Acid dissociation constants ( $K_a$ ) and rate constants for epoxidation of 2-halogeno-alcohols in aqueous sodium hydroxide at 25 °C and rate constants for formation of related aziridines by cyclization of 2-aminoethyl hydrogen sulphates in water at 75 °C

Substrate	$k_{\text{exp}}$ ( $\text{M}^{-1} \text{s}^{-1}$ )	$\text{p}K_a$ (estimated) †	$\text{p}K_a$ (by expt.)	$10^{15}K_a$ *	$k_{\text{cyc}}$ ‡ ( $\text{s}^{-1}$ )	Relative rates
$\text{ClCH}_2\text{CH}_2\text{OH}$	0.01	14.41	14.31 <sup>a</sup>	4.9	0.020	1
$\text{ClCH}_2\text{CHPhOH}$	0.655 <sup>b</sup>	13.56 <sup>c</sup>	13.64 <sup>b</sup>	27.5	0.24	12
$\text{ClCHPhCH}_2\text{OH}$	34.5 <sup>e</sup>	14.1 <sup>d</sup>		8.0	43	2150
$\text{BrCH}_2\text{CH}_2\text{OH}$	0.428 <sup>f</sup>	14.48		3.3	1.3	1
$\text{BrCH}_2\text{CHPhOH}$	29 <sup>g</sup>	13.53 <sup>c</sup>		29.5	9.8	7.5
	30.7 <sup>e</sup>	13.53 <sup>c</sup>			10.4	8.0
$\text{BrCHPhCH}_2\text{OH}$	1331 <sup>e</sup>	14.17 <sup>d</sup>		6.8	1960	1500
$\text{ICH}_2\text{CH}_2\text{OH}$	0.471 <sup>h</sup>	14.69		2.0	2.4	1
$\text{ICHPhCH}_2\text{OH}$	ca. 1000 <sup>e</sup>	14.38 <sup>d</sup>		4.2	2400	1000
$\text{NH}_2\text{CH}_2\text{CH}_2\text{OSO}_3^-$			8.97		$8.0 \times 10^{-6}$	1 <sup>i</sup>
$\text{NH}_2\text{CHPhCH}_2\text{OSO}_3^-$			8.14		$9.78 \times 10^{-6}$	1.22 <sup>f</sup>
$\text{NH}_2\text{CH}_2\text{CHPhOSO}_3^-$			8.52		$4.77 \times 10^{-4}$	59.2 <sup>f</sup>

\* From the experimentally determined  $\text{p}K_a$  where available. † See ref. 16;  $\text{p}K_a = 15.9 - 1.42 \sigma^*$  for  $\text{RCH}_2\text{OH}$ . ‡ From  $k_{\text{exp}}$  and  $K_{\text{eq}} = K_a/K_w$  where  $K_w = 10^{-14}$  and  $K_{\text{cyc}} = (k_{\text{exp}} \times K_w)/K_a$ .

<sup>a</sup> Ref. 17. <sup>b</sup> Ref. 8. <sup>c</sup>  $\text{p}K_a$  ca.  $15.9 - 1.42 \sigma^*_{\text{CH}_2\text{X}} - 1.42 \sigma^*_{\text{Ph}}$ . <sup>d</sup> Assume effect of  $\beta$ -Ph and  $\beta$ -X may be represented by addition of  $\sigma^*$  values for  $\text{R} = \text{PhCH}_2$  and  $\text{XCH}_2$  respectively. <sup>e</sup> This work. <sup>f</sup> Extrapolated from  $k_{\text{exp}} = 3.95 \text{ min}^{-1}$  at 10°,  $E_a = 21.9 \text{ kcal mol}^{-1}$ . <sup>g</sup> Ref. 6. <sup>h</sup> Extrapolated from  $k_{\text{exp}} = 3.84 \text{ min}^{-1}$  at 10°,  $E_a = 22.2 \text{ kcal mol}^{-1}$ . <sup>i</sup> Ref. 29.

This effect is not large in comparison with the rate enhancements attributed<sup>30,31</sup> to ethoxycarbonyl, acetyl, and to arylsulphonyl conjugation with incipient cyclopropanes.

The influence of vinyl substitution on cyclization of chlorohydrins has been determined by Kadesch.<sup>5</sup> It can be estimated (Table 8) that when  $\beta$  to the leaving group its effect is comparable to that of a phenyl group whereas in the  $\alpha$ -position the accelerating effect of a phenyl group is ten times that of a vinyl group.

TABLE 8

Cyclization of  $\beta$ -chlorohydrins in aqueous sodium hydroxide at 0 °C

Halohydrin	$10^4 k_{\text{exp}}/$ $1 \text{ mol}^{-1} \text{s}^{-1}$	$\text{p}K_a$	$10^{15}K_a$	$10^4 k^*_{\text{cyc}}/$ $\text{s}^{-1}$	Relative $k_{\text{cyc}}$
$\text{CH}_2=\text{CHCHClCH}_2\text{OH}$	1170 <sup>a</sup>	13.9 <sup>b</sup>	12.6	929	164
$\text{CH}_2=\text{CHCHOHCH}_2\text{Cl}$	283 <sup>a</sup>	13.5 <sup>b</sup>	31.6	89.5	15.8
$\text{CH}_2\text{ClCH}_2\text{OH}$	2.78 <sup>a</sup>	14.31 <sup>c</sup>	4.9	5.67	1

\* Based on  $K_a^{25}$  and  $k_{\text{exp}}^0$  where  $k_{\text{exp}} = k_{\text{cyc}} \times K_a/K_w$  and  $K_w = 10^{-14}$ .

<sup>a</sup> See ref. 5. <sup>b</sup> Estimated for 25 °C from ref. 16. <sup>c</sup> Ref. 12; 25 °C.

*Influence of Salt Concentration.*—Rates of reaction of  $\beta$ -chloro- $\beta$ -phenylethanol and its *p*-nitro-derivative in the presence of high concentrations of potassium chloride and potassium bromide have been measured. The results (Table 9) reveal the effect of added solute ions to be negligible. Similar absence of salt effect on rate of

TABLE 9

The effect of solute (S) on rates of reaction of  $\beta$ -chlorophenethyl alcohol (A) and its *p*-nitro-derivative (B) in aqueous sodium hydroxide at 25 °C

Reactant	S	[S]/M	$10^3 k^*/\text{s}^{-1}$
A †	KCl	0.2	1.53
	KCl	0.4	1.41
	KCl	1.0	1.43
	KBr	0.2	1.33
	KBr	0.4	1.37
	KBr	1.0	1.45
	KBr	1.0	1.51
	$\text{NaClO}_4$	0.1	1.61
	$\text{NaClO}_4$	0.2	1.92
B ‡	$\text{NaClO}_4$	0.4	2.43
	KCl	0.4	1.34
	KBr	0.4	1.41
	KBr	0.4	1.36
	$\text{NaClO}_4$	0.2	1.74

\* Pseudo-first-order rate constant at: † pH = 9.6; ‡ pH = 10.6.

## EXPERIMENTAL

*Materials.*—(a) *Styrene oxides.* Method A. The corresponding araldehyde (0.1 mol) and trimethylsulphonium bromide (0.1 mol) in dimethyl sulphoxide (DMSO) (60 ml) were treated with sodium hydride (0.125 mol) in DMSO (60 ml) dropwise during 45 min according to a literature procedure.<sup>32</sup>

Method B. According to the procedure of Guss<sup>33</sup> the corresponding aryl bromomethyl ketone was reduced by aluminium isopropoxide in isopropyl alcohol to give the

<sup>31</sup> A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1967, 808.

<sup>32</sup> V. Franzen and H. E. Driesen, *Chem. Ber.*, 1963, **96**, 1881.

<sup>33</sup> C. O. Guss, *J. Org. Chem.*, 1952, **17**, 678.

<sup>30</sup> A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1968, 67.

TABLE 10

Yield and physical properties of *m*- and *p*-substituted  $\beta$ -chlorophenethyl alcohols (prepared by ring opening the corresponding styrene oxide with HCl in chloroform)

Substituent	Yield (%)	B.p. (°C) (mmHg)	$n_D^{22}$	Molecular formula	Requires (%)		Found (%)		N.m.r. spectrum (CDCl <sub>3</sub> ) ( $\delta$ values)
					C	H	C	H	
H	75	98 (1.2)	1.5552	C <sub>8</sub> H <sub>9</sub> ClO					7.13 (5H, m), 4.8 (1H, t, <i>J</i> 7 Hz), 3.92 (1H, s, OH), 3.71 (2H, d, <i>J</i> 7 Hz, CH <sub>2</sub> )
<i>p</i> -Cl	61	107 (0.8)	1.5641	C <sub>8</sub> H <sub>9</sub> Cl <sub>2</sub> O	50.3	4.2	49.9	4.0	7.16 (4H, s), 4.8 (1H, t, <i>J</i> 7 Hz), 3.75 (2H, d, <i>J</i> 7 Hz), 3.55 (1H, s, OH)
<i>m</i> -Me	45	95 (1.0)	1.5458	C <sub>9</sub> H <sub>11</sub> ClO	63.3	6.5	63.45	6.8	7.0 (4H, m), 4.77 (1H, t, <i>J</i> 7 Hz), 3.73 (2H, d, <i>J</i> 7 Hz), 3.33 (1H, s, OH), 2.33 (3H, s, CH <sub>3</sub> )
<i>m</i> -MeO	58	125 (1.0)	1.5532	C <sub>9</sub> H <sub>11</sub> ClO <sub>2</sub>	57.9	5.9	57.6	6.2	6.5—7.25 (4H, m), 4.8 (1H, t, <i>J</i> 7 Hz), 3.77 (2H, d, <i>J</i> 7 Hz), 3.6 (3H, s, OMe), 3.46 (1H, s, OH)
<i>m</i> -NO <sub>2</sub>	55	149 (1.0)	1.5780	C <sub>8</sub> H <sub>8</sub> ClNO <sub>3</sub>	47.7	4.0	47.6	3.7	7.3—8.3 (4H, m), 5.03 (1H, t, <i>J</i> 6 Hz), 3.95 (2H, t, <i>J</i> 6 Hz), 3.48 (1H, s, OH)
<i>p</i> -NO <sub>2</sub>	77	161 (1.5)	1.5879	C <sub>8</sub> H <sub>8</sub> ClNO <sub>3</sub>	47.7	4.0	47.2	4.3	[7.42, 7.58, 6.0, 8.16 (4H, m)] 5.0 (1H, t, <i>J</i> 6 Hz), 3.93 (2H, d, <i>J</i> 6 Hz) 3.15 (1H, s, OH)

bromohydrin which was subsequently converted to the epoxide by reaction with aqueous sodium hydroxide.

The following styrene oxides were obtained by method A: *p*-methoxy (67%), m.p. 25°,  $\delta$  (CDCl<sub>3</sub>) 6.8, 6.94, 7.14, 7.29 (4H, m), 3.76 (3H, s, OMe), 3.76 (1H, m, ArCH), and 2.7—3.2 (2H, m, CH<sub>2</sub>) (lit., m.p. 16.5—17°; <sup>34</sup> lit., 20 ± 2°); <sup>35</sup> *p*-chloro (66%), b.p. 72° at 0.5 mmHg,  $n_D^{22}$  1.5480 (lit., <sup>36</sup> b.p. 108° at 13 mmHg,  $n_D^{20}$  1.5541); *p*-methyl (76%), b.p. 42° at 0.5 mmHg,  $n_D^{22}$  1.5275 (lit., <sup>22</sup> b.p. 40° at 0.1 mmHg,  $n_D^{18}$  1.5292); *m*-methoxy (80%), b.p. 73° at 0.5 mmHg,  $n_D^{24}$  1.5360 (lit., <sup>37</sup> b.p. 77° at 1 mmHg,  $n_D^{26}$  1.5377).

The following styrene oxides were obtained by method B: *m*-nitro, b.p. 101° at 0.5 mmHg,  $n_D^{23}$  1.5676 (lit., <sup>33</sup> b.p. 140—141° at 4 mmHg,  $n_D^{20}$  1.5698); *p*-nitro, m.p. 86° (from benzene-hexane); *p*-methyl, b.p. 54° at 1.2 mmHg,  $n_D^{25}$  1.5283 (lit., <sup>37</sup> b.p. 51.2° at 1 mmHg,  $n_D^{26}$  1.5277).

(b)  $\beta$ -Aryl- $\beta$ -halogenoethanols.  $\beta$ -Chloro- $\beta$ -phenylethanol. Styrene oxide (27 g, 0.224 mol) in dry chloroform (100 ml) was cooled to 0° and was treated with HCl (0.44M, 0.264 mol) in chloroform (600 ml) at 0°. After 20 min at room temperature the solution was washed with saturated sodium hydrogen carbonate, evaporated, and distilled to give the chloro-alcohol (26.1 g, 75%), b.p. 86° at 1 mmHg,  $n_D^{22}$  1.5552,  $\delta$  (CDCl<sub>3</sub>) 7.12 (5H, m), 4.8 (1H, t, *J* 7 Hz), 3.92 (1H, s, OH), and 3.71 (2H, d, CH<sub>2</sub>) (lit., <sup>38</sup> b.p. 97—99° at 1.2 mmHg,  $n_D^{25}$  1.5560).

$\beta$ -Chloro- $\beta$ -phenylethanol bearing *p*-MeO, *p*-Cl, *m*-Me, *m*-MeO, *m*-, or *p*-NO<sub>2</sub> substituents. Several attempts to prepare the *p*-methoxy-chloro-alcohol by modifications of the above procedure were unsuccessful.

Preparations of (i) *p*-Cl-, (ii) *m*-Me-, (iii) *m*-MeO-, (iv) *m*-NO<sub>2</sub>-, and (v) *p*-NO<sub>2</sub>-phenyl-chloro-alcohols were performed as for the parent compound, on a 5 g scale, and purification was by distillation. The yield, b.p., refractive index, and n.m.r. spectrum of each compound are in Table 10.

$\beta$ -Iodo- $\beta$ -phenylethanol. The iodo-alcohol was prepared in 60% yield by ring opening of styrene oxide with hydriodic acid by the method of Golumbic and Cottle <sup>39</sup> and had m.p. 77.5° (from benzene-hexane) (lit., <sup>39</sup> m.p. 78.5°).

<sup>34</sup> L. A. Strait, R. Ketchamp, D. Jambotkar, and V. P. Shah, *J. Amer. Chem. Soc.*, 1964, **86**, 4628.

<sup>35</sup> C. O. Guss, *J. Amer. Chem. Soc.*, 1952, **74**, 2561.

<sup>36</sup> T. Bergkvist, *Kgl. Fysiograf. Sällskap. Lund. Förh.*, 1948, **18**, 18 (*Chem. Abs.*, 1950, **44**, 1447b).

<sup>37</sup> R. Fuchs, *J. Amer. Chem. Soc.*, 1956, **78**, 5612.

<sup>38</sup> G. Bertini, F. Bottari, P. L. Ferrarini, and B. Macchia, *J. Org. Chem.*, 1965, **30**, 4091.

$\beta$ -Bromo- $\beta$ -phenylethanol. Previous attempts to prepare the pure bromo-alcohol have been unsuccessful [lit., <sup>40</sup> b.p. 96—130° at 2 mmHg (Found: Br, 35.5. C<sub>8</sub>H<sub>9</sub>BrO requires Br, 39.7%)]. The following procedure was successfully adopted. To a solution of styrene oxide (55.5 g) in ice cold pentane (120 ml) was added, dropwise with stirring, 48% hydrobromic acid (79 ml, 0.466 mol). The acid layer was separated, diluted with cold water (300 ml), and extracted with benzene. The extract was washed with ice-water, dried (MgSO<sub>4</sub>), and evaporated to give the crude product (50 g) which was purified by distillation. The bromo-alcohol (19 g), b.p. 112—118° at 0.5 mmHg,  $n_D^{26}$  1.5822 (Found: Br, 38.6%), was obtained, there being a considerable amount of high boiling residue.

(c) Styrene halogenohydrins ArCHOHCH<sub>2</sub>X. The following styrene bromohydrins were prepared from substituted phenacyl halides by aluminium isopropoxide reduction according to the procedure of Guss: <sup>33</sup> *m*-nitro, m.p. 42° (lit., <sup>41</sup> m.p. 42—43°), *p*-nitro, m.p. 88° (lit., <sup>42</sup> m.p. 86—87°); *p*-methyl, b.p. 109° at 2 mmHg,  $\delta$  (CDCl<sub>3</sub>) 7.0 (4H, s), 4.6 (1H, t, *J* 6 Hz), 3.62 (1H, s, OH), 3.29 (2H, d, *J* 6 Hz), and 2.18 (3H, s). Styrene bromohydrin which had b.p. 93° at 1.5 mmHg and  $n_D^{29}$  1.5672—1.5700 was stored in darkness under nitrogen at 0° (lit., <sup>43</sup> b.p. 100° at 1 mmHg). Styrene chlorohydrin had b.p. 79° at 1 mmHg,  $n_D^{27.5}$  1.5480 (lit., <sup>8</sup> b.p. 102° at 3 mmHg,  $n_D^{20}$  1.5512).

*Kinetics of Reaction of Arylhalogenoethanols in Aqueous Alkali.*—Reactions of the halogeno-alcohols with aqueous sodium hydroxide were followed by a pH-stat technique using a Sargent model D automatic recording titrator. Doubly distilled, deionized, CO<sub>2</sub>-free water (100 ml) was thermostatted in a titration vessel (150 ml capacity, 3 in diam.) with an air-tight cover which supported a thermometer, nitrogen inlet, titrant inlet, glass electrode, and calomel reference electrode. A slow stream of nitrogen was passed continuously and allowed to escape through a small vent.

The required pH was adjusted by addition of CO<sub>2</sub>-free

<sup>39</sup> C. Golumbic and D. L. Cottle, *J. Amer. Chem. Soc.*, 1939, **61**, 996.

<sup>40</sup> R. E. Buckles and J. E. Maurer, *J. Org. Chem.*, 1953, **18**, 1585.

<sup>41</sup> W. L. Evans and B. T. Brooks, *J. Amer. Chem. Soc.*, 1908, **30**, 404.

<sup>42</sup> C. O. Guss and H. G. Mautner, *J. Org. Chem.*, 1951, **16**, 887.

<sup>43</sup> H. Lund, *Ber.*, 1937, **70B**, 1520.

sodium hydroxide (0.3M) and the reaction was initiated by addition of the halogeno-alcohol (0.15M) in acetone (0.2—1 ml). The solution was stirred magnetically by a stirring box on which the vessel was supported. Constant pH was maintained by automatic addition of base solution (0.4—2.0 ml in all) and the pseudo-first-order rate constant was evaluated from the volume *versus* time record in the usual way.

In each case the substrate was completely miscible under these conditions. In general the styrene oxides were less soluble and separated as the reactions proceeded. It was demonstrated that this was without effect upon the titration procedure. The reaction rates were shown to be insensitive to low concentrations of acetone.

In a typical run the data to 95% completion of reaction were analysed by least-squares treatment in the usual way and a rectilinear first-order relationship was found. Where convenient the Guggenheim procedure<sup>44</sup> was adopted.

*Product Isolation.*—Products of reaction of *m*- and *p*-substituted phenylhalogenoethanols with aqueous sodium hydroxide were isolated as follows. To the halogeno-alcohol (2 g) in water (100 ml) sodium hydroxide (1M) was added

dropwise with stirring at a rate sufficient to maintain pH 11. In each case the theoretical amount (corresponding to epoxidation) of base was consumed. Chloroform (150 ml) was added and the aqueous layer was saturated with sodium chloride and extracted with a further three portions of chloroform. The combined extracts were washed once with water (50 ml), dried (MgSO<sub>4</sub>), and evaporated. Last traces of solvent were removed at reduced pressure (3 mmHg) and the product was weighed. In each case the n.m.r. spectrum of the product was identical to that of the corresponding oxide. The identity was confirmed by the i.r. spectrum which in each case revealed only a trace of impurity with O—H absorption. The refractive index of each product was in close agreement with that of the authentic oxide.

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<sup>44</sup> E. Guggenheim, *Phil. Mag.*, 1926, 2, 538.

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