ether in the presence of alumina–silica combinations, "solid phosphoric acid," aluminum chloride, sulfuric acid and hydrogen fluoride.

The determination of the isomer distribution in the resulting monoalkylates was not amenable to conventional methods, but it was accomplished by infrared and ultraviolet spectroscopy. The isomer distribution was found to be dependent upon the catalyst and/or conditions employed.

1-Ethylnaphthalene and 1-isopropylnaphthalene do not isomerize on simple distillation as reported by Tsukervanik and Terent'eva.

A laboratory apparatus for continuous alkylation under superatmospheric pressure was described which facilitated the otherwise difficult laboratory operation with a mixed gas–liquid feed.

Indan yielded condensation products of undetermined nature in the presence of alumina–silica and aluminum chloride.

PITTSBURGH, PENNSYLVANIA RECEIVED AUGUST 8, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

The Kinetics of the Reaction between the Ethylene Halohydrins and Hydroxyl Ion in Water and Mixed Solvents[1a]

BY C. L. MCCABE[1b] AND J. C. WARNER

The kinetics and course of the reaction between ethylene chlorohydrin and hydroxyl ion has been studied extensively in this[2a,2b] and other laboratories.[3a,3b,3c] The purpose of this study was to extend the investigation to the other halohydrins.

Experimental Method

The reactions were carried out in thermostats which held the temperature constant to within ±0.005° as measured by Beckman thermometers, which were calibrated against a National Bureau of Standards resistance thermometer. The rate of the reaction of the bromohydrin as well as iodohydrin was followed by determining halogen by the Volhard method; the rate with fluorohydrin was determined by following the hydroxyl ion concentration. In all experiments carbonate-free base was used and precautions were taken to exclude carbon dioxide during the course of the reaction.

The bromohydrin was prepared from ethylene oxide by a well established method.[4] Ethylene iodohydrin was prepared by the reaction between ethylene chlorohydrin and sodium iodide[5] in acetone solutions. Ethylene fluorohydrin was kindly furnished by the Chemical Corps, U. S. Army. The bromohydrin fraction used distilled at 51.0–51.1° at 4 mm., the iodohydrin at 75.0–75.2° at 5 mm. These distillations were carried out in a Vigreux flask with a variable take-off so that one could change receivers without admitting air. The iodohydrin is unstable and during the distillation iodine must be continually removed. Powdered silver was used for this purpose. The fluorohydrin as received was about 80% pure. It was further purified by two fractionations in a five-foot spiral wire column. The fraction used for the kinetic measurements boiled at 103.2° at 750 mm. On all three compounds an indication of the purity was obtained by allowing a weighed amount of the halohydrin to react to completion with excess base and then analyzing for halide ion. With bromohydrin as well as with iodohydrin, the amount of halide ion obtained in the reaction with base agreed within 0.1% with the calculated amount for the pure compounds.

When the ethylene fluorohydrin used in the kinetic experiments was allowed to react to completion with base, the purity indicated by fluoride analysis was 93.0% and that indicated by base consumed was 92.3%. Therefore, in calculating the fluorohydrin concentration, the substance was assumed to be 93.0% pure.

1,4-Dioxane was purified by refluxing over metallic sodium, followed by a distillation, and the methanol employed was redistilled. Carbon dioxide was excluded in each distillation.

The analysis of the amount of ethylene oxide formed from the reaction between hydroxyl ion and the ethylene halohydrins were carried out by a modification of Lubatti's method[6] in an enclosed flask with two compartments. In one, the base and halohydrin were allowed to react at room temperature, and after reaction was complete standard acid was added to the methyl orange end-point. The other compartment contained sufficient magnesium chloride hexahydrate to saturate the reaction mixture and enough alcoholic hydrochloric acid to make the reaction mixture about tenth normal. The reagents from the second compartment were transferred to the reaction mixture which was then allowed to stand for about thirty minutes. The amount of acid consumed in the conversion of ethylene oxide into halohydrin was calculated from the amount of standard base necessary to bring the mixture back to the methyl orange end-point.

The velocity constants were determined from the best straight line plot of the appropriate function of the concentration *versus* time. The unit of time for all constants reported in this paper is the minute.

Experimental Results

In Table I are summarized the velocity constants, activation energies and log B of the Arrhenius equation for the reactions of the various halohydrins with hydroxyl ion in water as solvent.

The rates of the reaction of these halohydrins with pure water have been investigated and are clearly negligible compared to the above rates of reaction with hydroxyl ion.[7]

Table II presents a summary of the velocity constants in water–methanol and water–dioxane mixtures for the various halohydrins. In columns five and six, velocity constants for the bromohy-

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(1) (a) Abstracted from a thesis submitted by C. L. McCabe to the Committee on Graduate Degrees, Carnegie Institute of Technology, in partial fulfillment of the requirements for the D.Sc. degree; (b) American Chemical Society Pre-doctoral Fellow, 1946–1947.

(2) (a) Winstrom and Warner, THIS JOURNAL, **61**, 1205 (1939); (b) Stevens, McCabe and Warner, *ibid.*, **70**, 2449 (1948).

(3) (a) Smith, *Z. physik. Chem.*, **81**, 339 (1912); (b) Brönsted, Kilpatrick and Kilpatrick, THIS JOURNAL, **51**, 428 (1929); (c) D. Porret, *Helv. Chim. Acta*, **27**, 1321 (1944).

(4) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 117.

(5) Wieland and Sakellarios, *Ber.*, **53**, 208 (1920).

(6) Lubatti, *J. Soc. Chem. Ind. (London)*, **51**, 361 (1932).

(7) Unpublished experiments from this Laboratory.

drin and the iodohydrin are compared to the velocity constant for the chlorohydrin in the two solvent mixtures.

Table I

Halohydrin	Temp., °C.	k, min.$^{-1}$	Activation energy, kcal.	Log B
CH_2OHCH_2F	30.0	0.00150	21.5	12.7
	40.0	.00508		
	60.0	.0380		
CH_2OHCH_2Cl	0	0.0167	23.3	16.8
	15	.153		
	25	.600		
	35	2.17		
CH_2OHCH_2Br	0.0	0.987	21.9	17.5
	5.0	2.03		
	10.0	3.95		
CH_2OHCH_2I	0.0	0.902	22.2	17.7
	5.0	1.83		
	10.0	3.84		

Table II

			Ratio: k_0 (X)/k_0 (Cl)		
Halohydrin	Water–dioxane	Water–methanol	in H_2O D = 88.4	in water-dioxane D = 64.2	in water-methanol D = 66.3
CH_2OHCH_2F	k_{60} = 0.042	k_{60} = 0.023	..	...	...
	D = 55.0	D = 55.0			
CH_2OHCH_2Cl	k_0 = 0.0538	k_0 = 0.00432	1	1	1
	D = 64.2	D = 66.3			
CH_2OHCH_2Br	k_0 = 4.58	k_0 = 0.447	59	85	103
	D = 64.2	D = 66.3			
CH_2OHCH_2I	k_0 = 5.94	k_0 = 0.600	54	110	138
	D = 64.2	D = 66.3			

In order to find out whether the same product was formed from the halohydrins in different solvents, analyses for ethylene oxide were carried out on the reaction product obtained from each of the halohydrins in water as solvent, and on the reaction products from ethylene bromohydrin and iodohydrin in dioxane–water and in methanol–water mixtures as solvents. These results are summarized in Table III.

Table III

Halohydrin	% Oxide in pure water	% Oxide in water–dioxane D = 66	% Oxide in water–methanol D = 64
CH_2FCH_2OH	72		
	79		
CH_2ClCH_2OH	94.1		
	96.2		
CH_2BrCH_2OH	92.4	91.8[a]	97.9
	94.6	96.3	96.8
	93.0		
CH_2ICH_2OH	94.6	99.6	98.1
	95.6	98.8	99.5

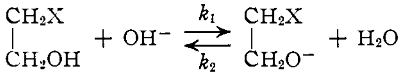
[a] The low result in this analysis may be explained by the fact that the reaction mixture was allowed to stand for twenty-four hours before analysis, instead of the usual two hours. Ethylene oxide may have been lost due to volatilization from solution and also by being hydrolyzed to glycol.

Although these data are not strictly quantitative, they definitely show that the major product in all cases is ethylene oxide. It was established that the other possible products, ethylene glycol or its methyl ether, are not converted into the halohydrin under the conditions which served to convert ethylene oxide.

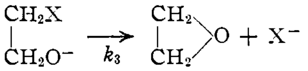
It is not surprising that analysis of the mixture obtained by treating ethylene fluorohydrin with hydroxyl ion yields lower percentages of ethylene oxide. This reaction is extremely slow giving more opportunity for the loss of oxide by volatilization. Furthermore, although the reaction of ethylene fluorohydrin with hydroxyl ion is more rapid ($k_{20} = 3.9 \times 10^{-4}$) than the hydrolysis of ethylene oxide to glycol[5] ($k_{20} = 2.10 \times 10^{-5}$), the hydration reaction becomes sufficiently important in the latter part of the fluorohydrin–hydroxyl ion reaction to account for the transformation of appreciable amounts of oxide to glycol.

Discussion of Results

The fact that ethylene oxide is the major product, that second order kinetics are followed, that the effect of changing the medium is of the same general type, and that the activation energies are approximately the same in the reaction between hydroxyl ion and the various halohydrins leads one to believe that the same mechanism prevails in each case. The mechanism which we have adopted is the one proposed by Winstein and Lucas[8] to explain the stereochemical relationships in reactions analogous to those studied in this investigation.



$$\begin{matrix} CH_2X \\ | \\ CH_2OH \end{matrix} + OH^- \underset{k_2}{\overset{k_1}{\rightleftarrows}} \begin{matrix} CH_2X \\ | \\ CH_2O^- \end{matrix} + H_2O \qquad (1)$$



(2)

Reaction (1) is a fast equilibrium step; reaction (2) is an attack of the negative oxygen of the intermediate ion on the carbon holding the halogen. This second step is a special type of the mechanism which has been denoted S_N2 by the English kineticists[9a] (denoted by Winstein[9b] as Type A with a velocity constant k_Δ).

In order to adequately discuss the experimental results of this investigation, it is necessary to consider the general case where there is present a solvent which consists of water and some other component.

On the basis of the mechanism given above, one can write

$$d[X^-]/dt = k_3[CH_3XCH_2O^-] \qquad (3)$$

Next express the concentration of $CH_2XCH_2O^-$ in terms of known concentrations and equilibrium constants, by making the definitions

$$K_{CH_2XCH_2OH} = \frac{a_{CH_2XCH_2O^-}\, a_{H^+}}{a_{CH_2XCH_2OH}} \qquad (4)$$

$$K_2 = a_{S^-} a_{H^+} / a_{SH} \qquad (5)$$

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(8) Winstein and Lucas, This Journal, **61**, 1576 (1939).

(9) (a) Hughes, *Trans. Faraday Soc.*, **37**, 606 (1941); (b) Winstein and Grunwald, This Journal, **70**, 833 (1948).

$$K_3 = a_{\mathrm{OH^-}}a_{\mathrm{H^+}}/a_{\mathrm{H_2O}} \qquad (6)$$

$$y = [a_{\mathrm{OH^-}}] + [a_{\mathrm{S^-}}] \qquad (7)$$

$$z = [\mathrm{OH^-}] + [\mathrm{S^-}] \qquad (8)$$

For water and SH the pure substances are taken as standard states; for all other species the reference states are infinite dilution in the particular solvent mixture under consideration.

This leads to the expression

$$[\mathrm{CH_2XCH_2O^-}] = \frac{K_{\mathrm{CH_2XCH_2OH}}\ [\mathrm{CH_2XCH_2OH}][z]f_{\mathrm{CH_2XCH_2OH}}f_{\mathrm{OH^-}}}{(\gamma_{\mathrm{SH}}\ [\mathrm{SH}]K_2 + K_3\ [\mathrm{H_2O}]\ \gamma_{\mathrm{H_2O}})f_{\mathrm{CH_2XCH_2O^-}}} \qquad (9)$$

if one assumes that $f_{\mathrm{OH^-}} \cong f_{\mathrm{S^-}}$. When Eqn. (9) is substituted in Eqn. (3), one obtains

$$k_{\mathrm{expt}} = \frac{k_3K_{\mathrm{CH_2XCH_2OH}}f_{\mathrm{CH_2XCH_2OH}}f_{\mathrm{OH^-}}}{([\mathrm{SH}]\gamma_{\mathrm{SH}}K_2 + [\mathrm{H_2O}]\gamma_{\mathrm{H_2O}}\ K_3)f_{\mathrm{CH_2XCH_2O^-}}} \qquad (10)$$

For the special case when pure water is the solvent, or K_2 is very small, *i. e.*, when SH is 1,4-dioxane, Eqn. (10) becomes

$$k_{\mathrm{expt}} = \frac{k_3K_{\mathrm{CH_2XCH_2OH}}f_{\mathrm{CH_2XCH_2OH}}f_{\mathrm{OH^-}}}{[\mathrm{H_2O}]\ \gamma_{\mathrm{H_2O}}\ K_3\ f_{\mathrm{CH_2XCH_2O^-}}} \qquad (11)$$

It has been assumed that the above mechanism and expressions are valid for X = F, Cl, Br and I.

Relative Rates.—Using the velocity constants in Table I, one may calculate the ratios of $k_{\mathrm{expt}}(\mathrm{X})$ to $k_{\mathrm{expt}}(\mathrm{I})$. They are Cl:Br:I—0.018:1.1:1. The observation of a maximum rate for the bromohydrin instead of the iodohydrin was unexpected; however, the following considerations are offered in explanation. Since we are dealing in ratios of k_{expt}, the concentration of water and some of the activity coefficients of Eqn. (11) will cancel. Therefore, the maximum rate must be explained through a maximum in $k_3K_1f_{\mathrm{CH_2XCH_2OH}}/f_{\mathrm{CH_2XCH_2O^-}}$ ($K_1 = K_{\mathrm{CH_2XCH_2OH}}/K_3$). The assumption is made that the activity coefficient ratio $f_{\mathrm{CH_2XCH_2O^-}}/f_{\mathrm{CH_2XCH_2OH}}$ is sensibly constant for X = Cl, Br, I. There is no obvious way to measure either k_3 or K_1 by direct experiment. One may obtain an approximate value for K_1 by an empirical method.[10] This yields the following values for the dissociation constants of the halohydrins as acids in pure water as the solvent at 25°: $K_{\mathrm{CH_2ClCH_2OH}} = 3.6 \times 10^{-17}$, $K_{\mathrm{CH_2BrCH_2OH}} = 2.7 \times 10^{-17}$, $K_{\mathrm{CH_2ICH_2OH}} = 1.7 \times 10^{-17}$. K_1 for each halohydrin will be the above values divided by the dissociation constant of water; therefore, the ratio of the K_1's will be: Cl:Br:I—2.1:1.6:1. From the data of Hughes and Shapiro[11] one may obtain ratios for the bimolecular velocity constants for the reaction between $\mathrm{OH^-}$ and the isopropyl halides, and these might be expected to be of approximately the same relative order of magnitude as the ratios of k_3 for the halohydrin reactions. These ratios are Cl:Br:I—0.012:0.43:1. If now these ratios are multiplied with those of K_1's, one obtains ratios of the k_3K_1's. These are Cl:Br:I—0.025:0.69:1. This still does not account for the maximum rate with the bromohydrin, but it does show the importance of the difference in the acid strengths of the halohydrins on the relative rates.

The empirical rule used for calculating acid strengths of the halohydrins was made for resonating acids and one would expect the non-resonating halohydrin acids to differ in strength to a greater degree than indicated by the rule.[10] Furthermore, the ratios of velocity constants taken from the data of Hughes and Shapiro are not strictly applicable to the present case. If more precise treatment along each of these lines were possible, it might be possible to account for the relative rates of reaction which have been observed in this investigation.

It is evident from Table II that the factor or factors which caused the maximum in rate to occur with bromohydrin have been decreased to such an extent that they are no longer in operation in the solvents of lower dielectric constant. Since we are dealing in ratios, all of the components of Eq. (10) cancel out except $k_3K_1f_{\mathrm{CH_2XCH_2OH}}/f_{\mathrm{CH_2XCH_2O^-}}$. At the present time we are unable to assess which of these terms has undergone the marked change.

Medium Effects.—In a previous investigation, a detailed study was made of the influence of the solvent medium on the rate of reaction of ethylene chlorohydrin with hydroxyl ion.[3] Among other solvent mixtures, 1,4-dioxane–water and methanol–water mixtures were used. In dioxane–water mixtures the expected steady increase in rate was observed as the percentage of dioxane in the solvent was increased; however, in methanol–water mixtures there was a regular decrease in rate as the percentage of methanol in the solvent was increased. As may be observed in Table II, these same effects were found in the present investigation for the reactions of fluorohydrin, bromohydrin and iodohydrin with hydroxyl ion.

The reaction between fluorohydrin and hydroxyl ion is so slow that solvent medium effects were studied only at 60°; however, it is possible to make a very interesting comparison of the medium effects observed in the reactions of the other three halohydrins at 0°. In spite of the fact that the addition of methanol to water decreases the rate while the addition of 1,4-dioxane to water increases the rate, the ratios $k_0(\mathrm{Cl})$, $k_0(\mathrm{Br})$, $k_0(\mathrm{I})$ are surprisingly alike in the two solvent mixtures while in pure water the ratio is quite different. It seems possible to explain this striking similarity in relative rates by referring to Eqn. (10). The quotient $K_{\mathrm{CH_2XCH_2OH}}/K_3$ in Eqn. (10) is equal to K_1 as used in the previous discussion of the mechanism in water as solvent. The ratio $K_{\mathrm{CH_2XCH_2OH}}/K_3$ should not be much affected by the addition of a non-aqueous solvent; therefore, it seems certain that, when SH is 1,4-dioxane, K_2 is so small that the principal effect of adding dioxane to water is the increase in k_3 as the dielectric constant is de-

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[10] "The Theory of Organic Chemistry," Branch and Calvin, Prentice-Hall, Inc., New York, N. Y., pp. 203-204.

[11] Hughes and Shapiro, *J. Chem. Soc.*, 1179 (1937).

creased[9]; however, when SH is methanol, it appears that K_2 is large enough that the effect of the term $K_2[CH_3OH]$ more than offsets the increase in k_3 brought about by the decrease in dielectric constant and, consequently, the experimental velocity constants decrease uniformly as methanol concentrations are increased.

When one considers the ratios of the experimental velocity constants $k_0(Cl)$, $k_0(Br)$, $k_0(I)$ for any solvent mixture of fixed composition from the standpoint of Eqn. (10), it seems safe to assume that the terms in the denominator and the activity coefficients in the numerator cancel to yield

$$k(Cl):k(Br):k(I) = k_3(Cl)K_{CH_2ClCH_2OH}:k_3(Br)K_{CH_2BrCH_2OH}:k_3(I)K_{CH_2ICH_2OH}$$

even though the rate constants at constant temperature widely differ because of difference in acid–base level. One is led to believe that the observed ratios of velocity constants are reasonable and that the observed similarity of these ratios in any solvent mixture of fixed dielectric constant should be expected. This is true because, as a first approximation, k_3 and $K_{CH_2XCH_2OH}$ should be about the same in media of the same dielectric constant.

By applying simple kinetic theory to (1) and (2) one can write

$$k_{expt} = k_1k_3/k_2[H_2O] \qquad (7)$$

Substituting in the Arrhenius equation and collecting terms, one has

$$k_{expt} = \frac{B_3B_1}{B_2[H_2O]}\, e^{-(\Delta E_3 + \Delta E_1 - \Delta E_2)/RT} \qquad (8)$$

$(\Delta E_3 + \Delta E_1 - \Delta E_2)$ is our experimental activation energy and $B_3B_1/B_2[H_2O]$ is our experimentally determined B. This collision term is responsible for the very low rate of the fluorohydrin compared to the other halohydrins (see Table I).

From Table I it is evident that the activation energies do not follow any regular sequence. This is probably due to the fact that the experimental activation energy is made up of three activation energies. It is apparent that $(\Delta E_1 - \Delta E_2)$ is essentially equal to the ΔH of reaction (1). From a consideration of the free energy change obtained from the equilibrium constants calculated earlier in this section and the assumption that ΔS in reaction (1) for X = Cl, Br and I is constant, one would expect that the ΔH would algebraically increase in the order Cl to Br to I. On the other hand, from analogy with the simple reactions in which halogen is displaced from alkyl halides by anion bases, one would expect ΔE_3 to decrease in the order Cl to Br to I. The latter effect may be somewhat modified in the halohydrin reactions, and to a different amount in each halohydrin, by the inductive effect of the negatively charged oxygen on the carbon–halogen bond. In any event, one sees the possibility of accounting for the general trend in the experimental activation energies by these opposing trends in ΔH and ΔE_3. Although these considerations provide a logical basis for a qualitative interpretation of the present data, their quantitative explanation must await further experimental data or a more precise theory of reaction rates.

Acknowledgment.—The authors wish to acknowledge the assistance of Mrs. Helen D. Cowan, who carried out most of the rate experiments and analyses reported in this paper.

Summary

1. Velocity constants, activation energies and the so-called frequency factors have been determined for the reactions between hydroxyl ion and ethylene fluorohydrin, bromohydrin and iodohydrin in water as solvent. Rate measurements with the fluorohydrin were made at 30, 40 and 60; with the bromohydrin and iodohydrin at 0, 5 and 10°.

2. Similar rate measurements were made with the fluorohydrin at 60° in 14.5% 1,4-dioxane (D = 55.0) and in 27.5% methanol (D = 55.0).

3. Rate measurements were made at 0° with the bromohydrin and the iodohydrin in 25.1% 1,4 dioxane (D = 64.2) and 43.1% methanol (D = 66.3).

4. For each halohydrin, the rate is higher in dioxane–water and lower in methanol–water than in pure water as solvent.

5. Reasonable explanations are offered for the influence of the different halogens on velocity constants and activation energies in water as solvent.

6. The observed effects of non-aqueous solvents on velocity constants have been qualitatively explained in terms of the various equilibria involved.

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