[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY]

On Cyclic Intermediates in Substitution Reactions. V. The Alkaline Hydrolysis of Tetramethylene Chlorohydrin

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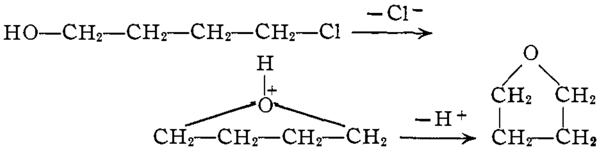
The rate of reaction of tetramethylene chlorohydrin with hydroxide ion has been determined. It has been established that (1) the rate of reaction is first order with respect to tetramethylene chlorohydrin and first order with respect to hydroxide ion; (2) the product of the reaction is tetrahydrofuran. The results are discussed in terms of a mechanism involving the formation and conversion of a chloroalcoholate ion to a cyclic ether. The results are compared with the formation of ethylene oxide from ethylene chlorohydrin and hydroxide ion.

Part IV of this series[1] presented a kinetic study on the reaction of some chlorohydrins with water which established that tetramethylene chlorohydrin reacts 1000 times as fast as ethylene chlorohydrin and 220 times as fast as trimethylene chlorohydrin. It also was shown that tetrahydrofuran was the main reaction product of tetramethylene chlorohydrin with water which presumably was formed by the expulsion of a proton from the cyclic intermediate I.



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In the present investigation the alkaline hydrolysis of tetramethylene chlorohydrin has been studied. The reaction is first order with respect to hydroxide ion and first order with respect to tetramethylene chlorohydrin. The kinetics of the reaction is easily followed by measuring the rate of release of the chloride ion. The reaction product is tetrahydrofuran.

Method of Rate Measurement.—The measurements were carried out in a water-bath in which the temperature was thermostatically controlled to ±0.02°. Ordinarily a quantity of chlorohydrin sufficient to make the concentration lie within the range 0.04–0.06 M was introduced into a 100-ml. volumetric flask which contained a known quantity of preheated standardized sodium hydroxide solution sufficient to make the final concentration of alkali 0.10 or 0.15 M. Water preheated to bath temperature was added to the mark and at convenient time intervals 10-ml. aliquots were removed with a pipet and immediately delivered into a solution of 5 ml. of 6 M HNO_3 and 30 ml. of distilled water. The unreacted chlorohydrin was extracted with three 10-ml. portions of chloroform and the chloride ion was determined by the Volhard method. In calculating the rate constants from the results of the titrations the first sample was taken as the starting point of the reaction.

Typical rate data for two different concentrations of sodium hydroxide are given in Table I. Table II summarizes the complete data on the second-order rate constants.

TABLE I

RATES OF ALKALINE HYDROLYSIS OF TETRAMETHYLENE CHLOROHYDRIN AT 30.00°

Time, min.	Mmole, Cl^-	$10^1 k_2$, l. moles^{-1} min.$^{-1}$	Time, min.	Mmole, Cl^-	$10^1 k_2$, l. moles^{-1} min.$^{-1}$
0.1405 N NaOH			0.0944 N NaOH		
10.00	0.073	1.70	12.03	0.066	1.67
19.33	.125	1.69	36.62	.160	1.73
29.36	.168	1.69	50.50	.195	1.70
40.20	.207	1.73	62.67	.222	1.71
51.36	.233	1.68	80.00	.254	1.73
61.25	.253	1.66	∞	.382	Mean 1.71
∞	.351	Mean 1.69			

TABLE II

RATE CONSTANTS FOR THE SECOND ORDER ALKALINE HYDROLYSIS OF TETRAMETHYLENE CHLOROHYDRIN

Chlorohydrin, N	NaOH, N	Temp., °C.	$10^2 k_2$, l. moles^{-1} min.$^{-1}$	Chlorohydrin, N	NaOH, N	Temp., °C.	$10^2 k_2$, l. moles^{-1} min.$^{-1}$
0.0412	0.1000	20	5.59	0.0446	0.1500	30	16.9
.0481	.1000	20	5.58	.0447	.1500	30	17.2
.0510	.1500	20	5.61	.0351	.1405	30	16.7
		Mean	5.59	.0382	.0944	30	17.1
						Mean	17.0

Experimental

Tetramethylene Chlorohydrin.—This compound was purchased from Matheson Chemical Company and redistilled. The fraction which distilled between 70–72° at 7 mm. was used.

Anal. Calcd. for C_4H_9OCl: Cl, 32.64. Found: Cl, 32.44.

Tetrahydrofuran.—One-tenth of a mole of tetramethylene chlorohydrin was dissolved in 150 ml. of 1.33 M sodium hydroxide and placed in a water-bath. After all the chlorine had been displaced the mixture was distilled and a fraction collected up to 98°. Redistillation of this fraction gave 6.8 g. of tetrahydrofuran (95%) boiling at 64–65°, n^{20} 1.4060.

Discussion

First, it is to be noted that the rate of the unimolecular reaction of tetramethylene chlorohydrin in water is of such magnitude as to make no appreciable contribution to the observed rates in the alkaline solutions. Thus, if the unimolecular constants at temperatures of 59.50° and 70.50° are used to calculate the temperature coefficient[1] the unimolecular rate constant at 30° can be estimated. The result is $k = 2.0 \times 10^{-4}$ min. From this one may conclude that the unimolecular reaction is negligible compared to the reaction with hydroxyl ion.

Second, the product from the bimolecular reaction is tetrahydrofuran. The formation of tetrahydrofuran can best be explained by a mechanism

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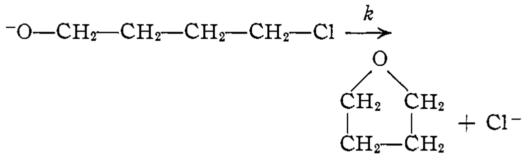
(1) H. W. Heine, A. D. Miller, W. H. Barton and R. W. Greiner THIS JOURNAL, **75**, 4778 (1953).

involving a two step process. The first step is a rapid equilibrium between hydroxide ion and the hydroxyl group of the chlorohydrin followed by a rate-determining displacement of chloride ion from the chloroalcoholate ion.

$$\mathrm{HO{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}Cl} + \bar{\mathrm{O}}\mathrm{H} \underset{}{\overset{K}{\rightleftarrows}} {}^{-}\mathrm{O{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}Cl} + \mathrm{H_2O} \quad (1)$$



(2)

$${}^{-}\mathrm{O{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}Cl} \xrightarrow{k} \mathrm{(CH_2)_4O} + \mathrm{Cl^-} \quad (2)$$

The rate equations would then be

$$\mathrm{d(Cl)/d}t = k({}^{-}\mathrm{O{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}Cl}) = kK(\mathrm{HO{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}Cl})({}^{-}\mathrm{OH})$$

The observed second-order rate constant k_2 is equal to kK and thus depends upon the acidity of the chlorohydrin and upon the reactivity of the chloroalcoholate ion formed. This mechanism has also been proposed by Winstein and Lucas[2] for the reaction of ethylene chlorohydrin with hydroxyl ion to form ethylene oxide.

It is of interest to compare the relative reactivities of ethylene chlorohydrin and tetramethylene chlorohydrin with hydroxide ion. This is best done by comparing the rates of reaction at a standard temperature and comparing the contributions made to the total free energy of activation by heat and entropy effects. These values may be estimated from the experimental data by means of Eyring's equation[3]

$$k = \frac{k'T}{n} e^{\Delta S^{\ddagger}/R} e^{-\Delta H^{\ddagger}/RT}$$

and are presented in Table III.

TABLE III

THERMODYNAMICS OF ACTIVATION, TOGETHER WITH ESTIMATED RATES OF REACTION AT 30.00° FOR ETHYLENE CHLOROHYDRIN AND TETRAMETHYLENE CHLOROHYDRIN WITH HYDROXIDE ION

Chlorohydrin	$\Delta H^{\ddagger}$, kcal.	$T\Delta S^{\ddagger}$, kcal.	$\Delta F^{\ddagger}$, kcal.	k_2, l. moles^{-1} min.$^{-1}$
Ethylene[a]	23.2	3.0	20.2	1.13
Tetramethylene	19.8	−1.5	21.3	1.72×10^{-1}

[a] Calculated from the data of C. L. McCabe and J. C. Warner, THIS JOURNAL, 61, 1205 (1939).

As shown in Table III the rate of formation of ethylene oxide is 7.5 times faster than the formation of tetrahydrofuran. This would seem surprising at first since the specific rate constant k for the conversion of the δ-chlorobutyl alcoholate ion to form the strainless five-membered tetrahydrofuran will certainly be much larger than the k value for the conversion of the β-chloroalcoholate ion to the strained ethylene oxide. This would be in harmony with the kinetic studies on the formation of cyclic imines and lactones. For example, Freundlich and Kroepelin[4] reported that the rate of cyclization of δ-bromobutylamine is 830 times as fast as the cyclization of β-bromoethylamine and Lane and Heine[5] noted that the rate of cyclization of γ-bromocaproate ion is 10^4 times as fast as the α-bromocaproate ion.

However, the observed second-order rate constants k_2 for the conversion of chlorohydrins to cyclic ethers are complex and include not only the specific rate constant k but also the acidity constant K of the chlorohydrins. The acidity constant K for ethylene chlorohydrin will be much larger (due to the enhanced acidity of the hydroxyl group by the presence of the halogen in the β-position) than the tetramethylene homolog. Winstein[2] has estimated the pK of ethylene chlorohydrin to be 16.9. The pK for ethanol is 18 and one would predict that the pK of tetramethylene chlorohydrin will be even higher. The large K value for ethylene chlorohydrin offsets the large k for the δ-chlorobutyl alcoholate ion and thus gives rise to the observed rates.

The faster rate of formation of ethylene oxide as compared to tetrahydrofuran seems to be attributable to the large difference in entropy (15 e.u.) between the two systems and not to any difference in the heat of activation which is more favorable by 3 kcal. for the formation of tetrahydrofuran. As a result of this entropy difference the free energy of activation is 1 kcal. less for the reaction of ethylene chlorohydrin with hydroxide ion.

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[2] S. Winstein and H. J. Lucas, THIS JOURNAL, **61**, 1576 (1939).

[3] S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 196.

[4] H. Freundlich and H. Kroepelin, *Z. physik. Chem.*, **122**, 39 (1926).

[5] J. F. Lane and H. W. Heine, THIS JOURNAL, **73**, 1348 (1951).