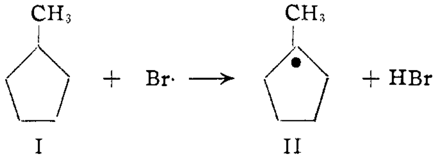
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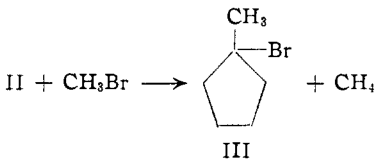
$$\mathrm{I} + \mathrm{CH_3\cdot} \longrightarrow \mathrm{II} + \mathrm{CH_4} \qquad (3)$$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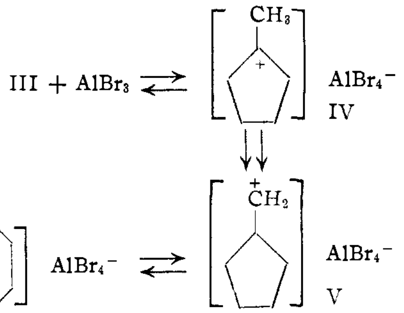
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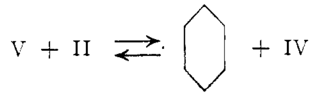
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EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY]

On Cyclic Intermediates in Substitution Reactions. IV. The Hydrolysis of Trimethylene- and Tetramethylene Chlorohydrins[1]

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The rates of hydrolysis for trimethylene- and tetramethylene chlorohydrins have been determined. It has been established that: (1) the rate of hydrolysis, as measured by the release of chloride ion, of trimethylene- and tetramethylene chlorohydrin is four times and a thousand times faster, respectively, than ethylene chlorohydrin; (2) the entropy of activation for tetramethylene chlorohydrin is more positive by about 6 e.u. than ethylene- or trimethylene chlorohydrin; (3) tetrahydrofuran is the main product of the hydrolysis of tetramethylene chlorohydrin.

Part I[2] of this series presented a study of the alkaline hydrolysis of some aliphatic bromoacids, in which the position of attachment of halogen ranged from α to γ, and which established that the reactivities increased in the order $\alpha < \beta \ll \gamma$. The increase of reactivity was interpreted as due to the increasingly strain-free character of the cyclic intermediate (lactone) formed.

It is of interest to investigate nucleophilic groups other than the carboxylate ion to see if they participate in the formation of cyclic intermediates as the distance between the nucleophilic group and the seat of substitution is increased. A suitable group of compounds for such a study would be the aliphatic chlorohydrins. In the present investigation the hydrolysis of trimethylene- and tetramethylene chlorohydrin has been studied. These substances are soluble in water at concentrations of 0.05–0.1 M and the kinetics of substitution (of oxygen for chlorine) are easily followed by measuring the release of the chloride ion. Here the hydroxyl group plays the role of the nucleophilic group.

The hydrolysis of ethylene chlorohydrin was investigated previously by Radulescu and Muresanu.[3]

Experimental

Trimethylene Chlorohydrin.—This compound was purchased from Matheson Chemical Company and redistilled. The fraction which boiled between 63–64° at 16 mm. was used in the rate studies.

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

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

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 0.05–0.1 M was introduced into a 100-ml. volumetric flask. Water preheated to the bath temperature was added 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 two 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 titration the first sample was taken as the starting point of the reaction.

Typical rate data for the two chlorohydrins are given in Table I. Table II summarizes the complete data on first-order rate constants of trimethylene chlorohydrin and tetramethylene chlorohydrin.

TABLE I

RATES OF HYDROLYSIS OF TRIMETHYLENE- AND TETRAMETHYLENE CHLOROHYDRINS

Time, min.	Vol. of 0.05 N $AgNO_3$, ml.	$10^4 k_1$, min.$^{-1}$	Time, min.	Vol. of 0.05 N $AgNO_3$, ml.	$10^2 k_1$, min.$^{-1}$
Trimethylene chlorohydrin, t = 86.30°			Tetramethylene chlorohydrin, t = 70.50°		
358.2	1.06	3.96	10.25	0.89	1.71
659.7	1.84	3.95	20.00	1.59	1.69
1270	3.29	4.16	30.09	2.23	1.71
2060	4.48	3.97	40.17	2.76	1.72
2581	5.13	3.96	50.17	3.22	1.74
3163	5.75	3.99	60.50	3.55	1.69
∞	8.02	Mean 4.00	∞	5.54	Mean 1.71

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(1) Presented at the American Chemical Society Meeting-in-Miniature at Philadelphia, Penna., Jan. 29, 1953.

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

(3) D. Radulescu and P. L. Muresanu, *Bull. soc. sci. cluj. Roumanie*, **7**, 129 (1932).

TABLE II

RATE CONSTANTS FOR THE HYDROLYSIS OF TRIMETHYLENE AND TETRAMETHYLENE CHLOROHYDRINS

Temp., °C.	10^4k_1, min.$^{-1}$	Mean	Temp., °C.	10^3k_1, min.$^{-1}$	Mean
Trimethylene chlorohydrin			Tetramethylene chlorohydrin		
72.00	1.05	1.03	50.30	2.24	2.18
	1.01			2.11	
	1.04			2.15	
	1.02			2.21	
86.30	4.00	4.03	59.50	5.88	5.92
	4.04			5.90	
	4.00			5.96	
	4.09			5.93	
96.60	10.7	10.5		5.92	
	10.5		70.50	17.1	17.2
	10.6			17.1	
	10.3			17.2	
	10.8			17.1	
				17.3	

Tetrahydrofuran.—Tetramethylene chlorohydrin (10.8 g.) was dissolved in 150 ml. of H_2O and placed in a water-bath at 40° for several weeks. The mixture was distilled and the first fraction collected up to 90°. Redistillation of this fraction yielded 5.3 g. of tetrahydrofuran boiling at 64–65°, n^{20}_{D} 1.4072 (reported value n^{21}_{D} 1.4076).

Discussion of the Results

For purposes of discussing the relative reactivities of the substances studied as well as ethylene chlorohydrin, it is desirable to compare the rates at a standard temperature and to compare the "thermodynamic" quantities of heat and entropy. These quantities may be estimated from the experimental data by means of Eyring's equation[4]

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

Accordingly values of the thermodynamic parameters of activation are presented in Table III together with the estimated values of the specific rate constants at 70.5°.

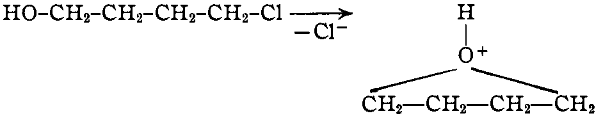
TABLE III

"THERMODYNAMICS" OF ACTIVATION, TOGETHER WITH ESTIMATED RATES OF HYDROLYSIS AT 70.5° FOR SOME CHLOROHYDRINS

Chlorohydrin	$\Delta H^{\ddagger}$, kcal.	$\Delta S^{\ddagger}$, e.u.	k, min.$^{-1}$
Ethylene[a]	24.5	−17.2	1.82×10^{-5}
Trimethylene	23.9	−16.2	7.79×10^{-5}
Tetramethylene	21.9	−11.1	1.71×10^{-2}

[a] Calculated from the data of Radulescu and Muresanu.[3]

It is to be noted that the rates of hydrolysis as measured by the release of chloride ion increase about four times as the chlorine is removed from the β-carbon atom in ethylene chlorohydrin to the γ-carbon atom in trimethylene chlorohydrin and increases a thousand-fold when the chlorine is removed to the δ-position in tetramethylene chlorohydrin. The large increase in reactivity of the chlorine atom in the case of tetramethylene chlorohydrin is, in our opinion, attributable primarily to the participation of the hydroxyl group in the formation of the transition state through the cyclic intermediate I, *i.e.*



I

The entropy values indicate that when the reactant is converted to the transition state, there is a greater degree of randomness in the case of tetramethylene chlorohydrin (−11 e.u.) than in the cases of ethylene chlorohydrin (−17 e.u.) and trimethylene chlorohydrin (−16 e.u.). The higher entropy value for tetramethylene chlorohydrin could be due to a freeing of water molecules which were oriented stiffly around the hydroxyl group. This, of course, can only occur if the hydroxyl group itself effects the substitution with attendant formation of a cyclic intermediate. A study of the composition of products in the hydrolysis of tetramethylene chlorohydrin might yield some evidence for a cyclic intermediate; for example, the intermediate I could stabilize itself by ejecting a proton to form tetrahydrofuran. A 73% yield of tetrahydrofuran was obtained when a 1.5 *M* solution of tetramethylene chlorohydrin was hydrolyzed at 40°.

The lower entropy values observed for ethylene chlorohydrin and trimethylene chlorohydrin indicate that the substitution process proceeds, as suggested previously by Cowan, McCabe and Warner[5] for the system ethylene chlorohydrin, by means of a SN2 reaction with water, *i.e.*

$$\mathrm{HO{-}CH_2{-}CH_2{-}Cl + H_2O \longrightarrow HO{-}CH_2{-}CH_2{-}OH + H^+ + Cl^-}$$

In this event the hydroxyl group would not be involved directly in the formation of the transition state. This is in agreement with the observation that ethylene glycol is the only product formed in the hydrolysis of ethylene chlorohydrin and in our observation that no trimethylene oxide could be isolated in the hydrolysis of trimethylene chlorohydrin. The slight increase in rate of trimethylene chlorohydrin over ethylene chlorohydrin suggests some participation of the hydroxyl group in this system.

The results indicate that in the hydrolysis of ethylene chlorohydrin and trimethylene chlorohydrin a SN2 reaction with water accounts for most, if not all, of the substitution process, but in the case of tetramethylene chlorohydrin the major portion of the substitution proceeds through an intramolecular SN2 process with the formation of a cyclic intermediate, the remainder proceeding by reaction with water.

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[4] 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.

[5] H. D. Cowan, C. L. McCabe and J. C. Warner, THIS JOURNAL, **72**, 1194 (1950).