

Kinetics and Mechanisms of Dehydrochlorination Reactions of Simple 1,2-Chlorohydrins in Aqueous Sodium Hydroxide Solutions

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The reactions of 2-chloroethanol (1), 2-chloro-1-propanol (2) and 1-chloro-2-propanol (3) in aqueous sodium hydroxide solutions at different temperatures were studied. Dehydrochlorination of each compound involves, in addition to the base-catalyzed reaction, a detectable neutral reaction. The relative rates of 1, 2, and 3 at 293 K are 1, 9.3 and 24.6 for the hydroxide ion-catalyzed, and 1, 1.4 and 6 for the neutral reaction.

The reactivity of 1,2-chlorohydrins depends particularly on the type and location of substituents in the molecule. Alkyl substitution markedly increases the reactivity of 2-chloroethanol under both basic and acidic conditions.¹⁻⁴ Information on the reactions between alkyl-substituted 1,2-chlorohydrins and hydroxide ion is mainly based on the studies of Ewans¹ and Smith *et al.*² Winstein and Lucas⁵ suggested the mechanism for this reaction which was confirmed later by Swain *et al.*⁶ These studies and subsequent results have been summarized by Frost and Pearson.⁷ Other interesting results in this field are given by Myszkowski and his group^{4,8-11} whose studies have concerned the synthesis of short-chain 1,2-chlorohydrins and their reactions under alkaline and acidic conditions. Recently, two reports from this laboratory considering the dehydrochlorination of long-chain diastereoisomeric 1,2-chlorohydrins, such as *threo*- (4) and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acids (5) found out in addition to the base-catalyzed reaction an appreciable contribution from a neutral reaction.^{12,13} No attention has previously been paid to the contribution of neutral reaction in the basic dehydrochlorination of 1,2-chlorohydrins. In the present paper

the dehydrochlorination reactions of 2-chloroethanol (1) and its methyl derivatives, 2-chloro-1-propanol (2) and 1-chloro-2-propanol (3), were investigated in aqueous sodium hydroxide solutions in order to clarify the extent of neutral reaction and the temperature dependence of both the base-catalyzed and neutral reactions.

EXPERIMENTAL

Materials. Commercial 2-chloroethanol (1) (British Drug Houses Ltd.) was distilled over anhydrous calcium sulfate with sodium carbonate added to remove traces of acid. The fraction of b.p. 401–402 K/101 kPa and n_D^{20} 1.4420 was collected (lit.¹⁴ 401 K/101 kPa, n_D^{20} 1.4419). 2-Chloro-1-propanol (2) was prepared from 2-chloropropionyl chloride (E. Merck AG) by reduction with LiAlH_4 as suggested by Ballinger and Long.¹⁵ The product had b.p. 341–343 K/10 kPa and n_D^{20} 1.4365 (lit.¹⁵ b.p. 311 K/1.7 kPa, n_D^{25} 1.4362). 1-Chloro-2-propanol (3) was synthesized from chloroacetone (E. Merck AG) by reduction with LiAlH_4 . The product had b.p. 323–330 K/4.1 kPa and n_D^{20} 1.4365 (lit.¹⁶ 338 K/10 kPa, n_D^{20} 1.4366).

Kinetics. The kinetic measurements were carried out at 4 to 5 temperatures in aqueous NaOH solutions (0.01 to 0.05 mol dm⁻³), the substrate concentration being 0.01 mol dm⁻³. The reactions were followed by titrating the chloride ion formed with dilute $\text{Hg}(\text{NO}_3)_2$ solution in aqueous methanol (80 % v/v) as reported earlier.^{12,13}

Evaluation of the rate coefficients. It has been pointed out previously^{12,13} that in alkaline water solutions the rate of dehydrochlorination of 1,2-chlorohydrins can be presented as follows:

$$\text{Rate} = (k_0 + k_{\text{HO}^-})[\text{S}] \quad (1)$$

Table 1. Values on the rate coefficients and their standard deviations for the base-promoted (k_{HO}) and neutral (k_0) dehydrochlorination of 2-chloroethanol (1) at different temperatures. For the definition of [S], $[\text{HO}^-]$, \bar{k}_t , and \bar{c}_t see the text.

Temp./ K	$10^3[\text{S}]/$ mol dm ⁻³	$10^3[\text{HO}^-]/$ mol dm ⁻³	$10^3\bar{k}_t/$ min ⁻¹	$10^3\bar{c}_t/$ mol dm ⁻³	$10^5k_0/$ s ⁻¹	$10^3k_{\text{HO}}/$ dm ³ mol ⁻¹ s ⁻¹
303	10.0	25.1	2.58	22.8	9 ± 3	15.2 ± 0.9
	10.0	33.1	3.25	29.5		
	10.0	39.8	3.81	36.3		
308	10.1	31.8	5.71	28.5	14 ± 5	28.2 ± 1.5
	9.8	36.6	6.38	33.2		
	9.9	47.1	8.26	43.7		
313	9.8	19.4	5.28	15.5	18 ± 3	47.0 ± 1.1
	9.8	23.6	6.62	19.5		
	9.8	24.3	6.85	20.5		
	10.0	32.2	9.11	28.3		
	10.0	32.3	9.04	28.0		
	9.8	40.1	11.1	36.0		
318	9.8	16.5	8.20	12.8	23 ± 6	88.8 ± 2.9
	9.8	21.7	11.1	18.2		
	9.8	26.2	13.1	22.6		
	9.8	32.2	16.8	28.8		
323	9.8	12.2	8.29	8.01	29 ± 8	137 ± 6
	9.8	15.1	11.2	11.2		
	9.8	17.2	13.0	14.0		
	9.8	20.7	15.7	16.9		

Table 2. Values of the rate coefficients and their standard deviations for the base-promoted (k_{HO}) and neutral (k_0) dehydrochlorination of 2-chloro-1-propanol (2) at different temperatures. For the definition of [S], $[\text{HO}^-]$, \bar{k}_t , and \bar{c}_t see the text.

Temp./ K	$10^3[\text{S}]/$ mol dm ⁻³	$10^3[\text{HO}^-]/$ mol dm ⁻³	$10^3\bar{k}_t/10^4$ min ⁻¹	$10^3\bar{c}_t/$ mol dm ⁻³	$10^5k_0/$ s ⁻¹	$10^3k_{\text{HO}}/$ dm ³ mol ⁻¹ s ⁻¹
283	10.02	24.94	1.74	22.9	(1 ± 1) ^a	12.3 ± 0.4
	10.02	34.17	2.46	32.3		
	10.02	39.52	2.84	37.25		
	10.02	44.61	3.18	40.6		
288	10.02	24.94	3.43	22.8	3 ± 2	23.5 ± 0.5
	10.01	34.16	4.65	31.9		
	10.02	39.50	5.49	37.7		
	10.02	44.45	6.22	42.5		
293	10.02	10.43	2.41	8.05	7 ± 2	42.0 ± 0.9
	10.02	16.51	4.15	14.4		
	10.02	25.02	6.00	22.5		
	10.02	34.18	8.46	31.8		
298	10.02	10.42	4.47	8.07	13 ± 2	76.5 ± 0.7
	10.01	16.51	7.22	14.0		
	10.02	25.00	10.9	22.4		
	10.02	34.18	15.2	31.4		

^a Not used for deriving ΔH^\ddagger , ΔS^\ddagger , and ΔG^\ddagger .

Table 3. Values of the rate coefficients and their standard deviations for the base-promoted (k_{HO}) and neutral (k_0) dehydrochlorination of 1-chloro-2-propanol (3) at different temperatures. For the definition of [S], [HO⁻], \bar{k}_t , and \bar{c}_t see the text.

Temp./ K	$10^3[\text{S}]/$ mol dm ⁻³	$10^3[\text{HO}^-]/$ mol dm ⁻³	$10^3\bar{k}_t/$ min ⁻¹	$10^3\bar{c}_t/$ mol dm ⁻³	$10^5k_0/$ s ⁻¹	$10^3k_{\text{HO}}/$ dm ³ mol ⁻¹ s ⁻¹
278	10.02	24.9	3.01	23.0	$(1.5 \pm 0.8)^a$	21.1 ± 0.2
	10.02	34.1	4.11	31.9		
	10.02	39.4	4.74	36.9		
	10.02	44.5	5.48	42.5		
283	10.02	24.9	5.53	23.4	6 ± 4	36.9 ± 1.3
	10.02	34.1	7.52	32.0		
	10.02	39.4	8.64	37.5		
288	10.02	10.4	4.28	8.56	10 ± 2	71.0 ± 1.2
	10.02	13.1	5.14	10.8		
	10.02	16.5	6.79	14.2		
	10.02	24.9	10.1	22.7		
	10.01	34.1	14.1	31.5		
293	10.02	10.4	7.52	8.51	28 ± 6	113 ± 5
	10.02	13.1	9.01	10.9		
	10.02	15.4	10.7	13.2		

^a Not used for deriving ΔH^\ddagger , ΔS^\ddagger , and ΔG^\ddagger .

where k_0 is the rate coefficient for the neutral and k_{HO} for the hydroxide ion-catalyzed reaction. The base and substrate concentrations are [HO⁻] and [S], respectively. By following the reactions at several initially different base concentrations it was possible to evaluate the values of k_0 and k_{HO} from eqn. (2).

$$\bar{k}_t = k_0 + k_{\text{HO}}\bar{c}_t \quad (2)$$

The average base concentrations \bar{c}_t for each run were calculated using a program written for an IBM 1130 and/or DEC 10 computer based on the trapezoidal rule.^{17,18}

$$\bar{c}_t = c_0 - \frac{1}{2t} \sum_{j=1}^i (x_j + x_{j-1})(t_j - t_{j-1}) \quad (3)$$

where c_0 is the initial base concentration and x_j the amount of chloride ion formed at time t_j . The average rate coefficients \bar{k}_t for each run were obtained from the standard first-order rate equation involved in the program. The values of k_0 and k_{HO} obtained from eqn. (2) by the method of least squares are presented in Tables 1 to 3.

RESULTS AND DISCUSSION

The present results show that the dehydrochlorination of 2-chloroethanol (1), 2-chloro-1-propanol (2), and 1-chloro-2-propanol (3)

in aqueous sodium hydroxide solutions involves the base-catalyzed reaction and a simultaneous neutral reaction similar to that described earlier for diastereoisomeric long-chain 1,2-chlorohydrins, *threo*- (4) and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acids (5).¹³ The course of this neutral reaction is not yet clear but experiments under initially neutral conditions may solve this problem. The rate coefficients at different temperatures for 1-3 are collected in Tables 1 to 3 and the values of thermodynamic functions of activation evaluated from them by the method of least squares are in Table 5. The rates relative to that of 1 at 293 K are listed in Table 4.

Dehydrochlorination of 1 promoted by hydroxide ion is a bimolecular displacement reaction, which follows second-order kinetics,

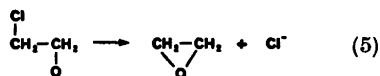
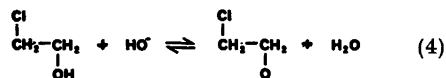


Table 4. Relative rates at 293 K for the base-catalyzed and neutral dehydrochlorination reactions of some 1,2-chlorohydrins in aqueous sodium hydroxide solutions.

Compound		Relative rate	
		Base catalysis	Neutral reaction
2-Chloroethanol	(1) ^a	1	1
2-Chloro-1-propanol	(2)	9.3	1.4
1-Chloro-2-propanol	(3)	24.6	6.0
<i>threo</i> -9(10)-Chloro-10(9)-hydroxyoctadecanoic acid	(4) ^b	2.3	4.6
<i>erythro</i> -9(10)-Chloro-10(9)-hydroxyoctadecanoic acid	(5) ^b	10.4	11.3

^a The values for $k_{\text{HO}} = 0.00045 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ and for $k_0 = 0.00005 \text{ s}^{-1}$ at 293 K are evaluated from the Arrhenius plot. ^b Ref. 13.

Table 5. Values of thermodynamic functions of activation with their standard deviations at 298 K for dehydrochlorination of some 1,2-chlorohydrins in aqueous sodium hydroxide solutions.

Compound	$\Delta H^\ddagger /$ kJ mol ⁻¹	$\Delta S^\ddagger /$ J mol ⁻¹ K ⁻¹	$\Delta G^\ddagger /$ kJ mol ⁻¹
Base catalysis			
1	88 ± 2	10 ± 8	84.9 ± 0.1
2	82 ± 1	10 ± 3	79.4 ± 0.02
3	75 ± 3	-8 ± 10	77.1 ± 0.1
4 ^b	70 ± 2	-43 ± 7	83.1 ± 0.03
5 ^b	55 ± 2	-84 ± 6	79.6 ± 0.04
Neutral reaction			
1	45 ± 3	-173 ± 11	96.8 ± 0.2
2	(99 ± 8) ^a	(12 ± 27) ^a	95.1 ± 0.2
3	(102 ± 22) ^a	(34 ± 78) ^a	91.7 ± 0.8
4 ^b	58 ± 5	-118 ± 16	92.8 ± 0.1
5 ^b	37 ± 2	-182 ± 8	90.9 ± 0.04

^a Enthalpy and entropy differences are not very significant in these cases. ^b Ref. 13.

first-order in hydroxide ion concentration and first-order in substrate concentration. According to Winstein and Lucas,⁵ this intramolecular substitution (S_{Ni}) is consistent with the above mechanism which has been supported by Swain *et al.*⁶ Stereochemically the above reaction, however, was shown to be a *trans* process only recently.¹³ The kinetic studies on the reactions of 2-chloroethanol (1) and its methyl and ethyl derivatives with hydroxide ion revealed that alkyl substituents appreciably increase the total reaction rate.¹⁻³ A similar increase in the reactivity of 1,2-chlorohydrins has also been observed under acidic conditions.⁴ The neighboring alkyl groups increase

the stability of cyclic compounds accelerating the ring formation.¹⁹ Winstein and Grunwald²⁰ have also suggested that the beneficial influence of alkyl substitution is reflected in the epoxide ring closure. In the closure of small rings the steric hindrance due to substituents is decreased.²¹ This is revealed by the observation that an alkyl substituent at either end of the closing chain will facilitate ring formation,²² and by the study described in the previous report from this laboratory.¹³ Our investigation showed that the difference in dehydrochlorination rates of vicinally disubstituted diastereoisomeric *threo*- (4) and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acids (5) is mainly

due to the different ground state energies of the reactive HO,Cl-*trans* conformations.¹³ The rate ratio obtained experimentally for 4 and 5 and that estimated for the vicinal dimethyl derivatives¹³ of 1 are very close to each other which indicates that both vicinal alkyl substituents in 2-chloroethanol (1) increase the reaction rate but the length of the alkyl chains is not an important factor (Table 4).

In the unsymmetrical case the effect of alkyl substitution is not obvious because it is greatly dependent on the location, size and kind of substituents. For example, the ethyl group is more effective than the methyl group in the promoting of epoxide ring formation.^{2,3} The alkyl or chloroalkyl groups at C-1 have greater influence than those at C-2 on the reactivity of 2-chloroethanols under basic^{1-3,10} or acidic⁴ conditions. The situation is reserved when two alkyl groups are attached to the same carbon atom^{2,3,21} or when the substituent is a vinyl group.²³

The effect of alkyl substituents to promote the reactivity of the chlorine atom in 1,2-chlorohydrins is opposite to their effect on the rate of bimolecular substitution which is usually decreased by alkyl groups. The present results (Tables 1-4) show that methyl-substituted 2-chloroethanols (2,3) have greater reactivity than 2-chloroethanol (1), both in base-catalyzed and in neutral reactions. In both cases the rate increase is much larger when the methyl group is attached to the carbon carrying the hydroxyl group (compound 3). That the behavior of the unsymmetrical 1,2-chlorohydrins, 2 and 3, differs from that of the unsubstituted compound, 1, or of the vicinally disubstituted long-chain 1,2-chlorohydrins, 4 and 5, is clearly seen from Fig. 1 (keeping in mind that the present method does not lead to very accurate k_0 values although it improves the precision of k_{HO} rate coefficients) which shows the dependence of the ratio of k_{HO} to k_0 on temperature. For 1 the value of this ratio increases significantly with temperature, revealing that the rate of the hydroxide ion-catalyzed reaction is more dependent on temperature than that of the neutral reaction. A similar but weaker effect was observed for 4 and 5^{12,13} whereas the monomethyl-substituted 2-chloroethanols, 2 and 3, behave oppositely.

According to a bimolecular displacement

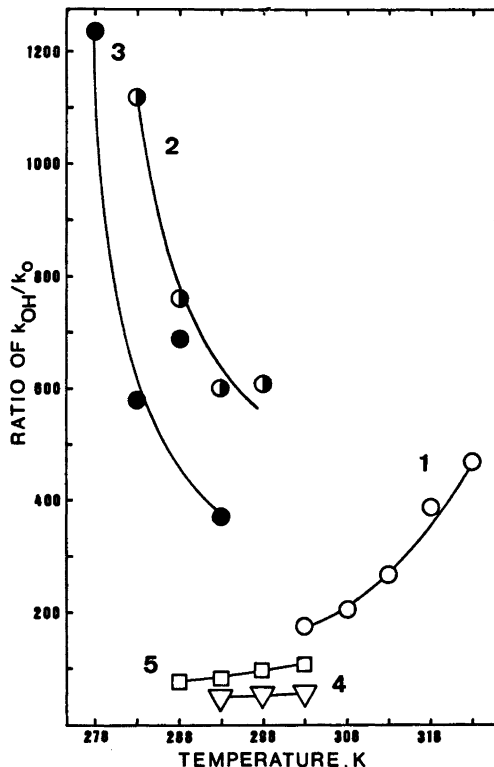
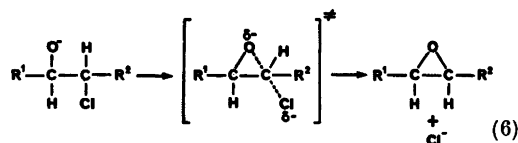


Fig. 1. Rate ratio k_{HO}/k_0 as a function of temperature for 2-chloroethanol (1), 2-chloro-1-propanol (2), 1-chloro-2-propanol (3), threo-9(10)-chloro-10(9)-hydroxyoctadecanoic acid (4), and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acid (5).

reaction, epoxides may be formed from 2 ($R^1 = H$, $R^2 = CH_3$) or 3 ($R^1 = CH_3$, $R^2 = H$) through the transition state given in (6). It is



also known¹³ that the relative populations of the reactive HO,Cl-*anti* conformations of 2 and 3 are about the same. Thus the difference between the rates of 2 and 3 may be mainly attributed to the different polar influences of the methyl group when it is bonded either at C-1 or C-2 in 2-chloroethanol. Compound 3 was more reactive than 2 both in base-catalyzed and

neutral reactions. Therefore one can assume that the polar effect of the methyl group plays a significant role also in the latter reaction.

As to the values of thermodynamic functions of activation they are comparable for 1–3 in the base-catalyzed reaction but only ΔG^\ddagger is defined accurately enough for the neutral reactions to be mechanistically conclusive.

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