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Chlorinated Long-chain Fatty Acids. Their Properties and Reactions. V. Alkaline Dehydrochlorination of Sodium *threo*- and *erythro*-9(10)-Chloro-10(9)-hydroxyoctadecanoates

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The base-catalyzed dehydrochlorination of *threo*- and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acids in water and in ethylene glycol-water mixtures has been studied. The reactions followed apparent second-order kinetics and *threo*- and *erythro*-isomers formed *cis*- and *trans*-9,10-epoxyoctadecanoic acids, respectively. In water solutions the contribution of the water reaction was very significant besides the hydroxide ion catalysis but no catalytic effect of solvent was found in aqueous ethylene glycol mixtures, which contained 16.6 mol % of water. The rate ratios of *threo*- and *erythro*-chlorohydroxyoctadecanoic acids determined for the base catalysis, for the water reaction, and for the reaction in aqueous ethylene glycol at 25°C were 0.45, 0.50, and 0.35, respectively.

The alkaline dehydrochlorination of sodium *threo*-9,10-dichlorooctadecanoate (I) (chlorinated oleic acid [1a]) may take place by a bimolecular elimination (E2) or a substitution (S_N2) mechanism. Earlier results [1b,1c] showed, however, that the alkaline dehydrochlorination of I very likely proceeds by the E2 mechanism in water and ethylene glycol-water mixtures. However, the occurrence of the substitution reaction could not be fully excluded.[1b,1c] To solve this problem, *threo*-9(10)-chloro-10(9)-hydroxyoctadecanoic acid (II), the product of the alkaline S_N2-type dehydrochlorination of I,[1c] was prepared and the rate of its alkaline dehydrochlorination was determined and compared with the rate of removal of the second chlorine atom from I.

EXPERIMENTAL

The NMR-spectra were taken for 10 – 15 % solutions of the samples in carbon tetrachloride using a 60 MHz Perkin Elmer R-10 spectrometer. The chemical shifts are given in ppm downfield from tetramethylsilane (TMS) which was used as internal reference.

The chlorine contents and melting points were determined as reported earlier.[1a]

Synthesis. threo-9(10)-Chloro-10(9)-hydroxyoctadecanoic acid (II) and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acid (III) were synthesized according to Swern *et al.*[2,3] Oleic acid (25 g) (Fluka AG, 96 % by GLC) and elaidic acid (12 g) were oxidized with peracetic acid to *cis*- (22.2 g) and *trans*-9,10-epoxyoctadecanoic acids (13.7 g), respectively. Ring opening (with HCl) of these epoxides yielded 11.8 g (45 %) of II and 7.3 g (51 %) of III after three crystallizations from hexane (1 g of acid in 4 ml of solvent). The *threo* compound II melted at 37 – 39°C (lit.[3-5] 39°; 38 – 41°; 35 – 41°C) and its chlorine content based on six determinations was 10.54 ± 0.09 % (calc. 10.59 %). The *erythro* compound III melted at 53 – 54°C (lit.[3-5] 58.0 – 58.8°; 52 – 57°; 53 – 58°C) and its chlorine content was 10.25 ± 0.13 % (calc. 10.59 %). The wide melting ranges are due to the fact that both stereoisomers were mixtures of two isomeric acids (9,10 and 10,9) that have different melting points.[6]

Elaidic acid (m.p. 42.5°C, lit.[7] 43 – 44°C) was prepared from oleic acid.[7]

Kinetic measurements. The alkaline dehydrochlorinations of II and III were carried out in water and ethylene glycol-water mixtures as described earlier [1b,1c] except that only single samples were taken at intervals (Tables 1 and 2). The effects of base concentration and the ethylene glycol content of the solvent on the reaction rate were also studied (Fig. 1; Table 1). The substrate concentrations in the reaction mixtures varied from 0.020 to 0.021 mmol/g of solvent.

Table 1. Rate coefficients of the alkaline dehydrochlorination of sodium *threo*- and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoates in aqueous ethylene glycol mixtures.

Temp.[a] °C	10^2 [OH^-] mol kg^{-1}	Water content mol fraction	wt. %	10^3 k_{OH} kg mol^{-1} s^{-1}
threo-*9(10)-Chloro-10(9)-hydroxyoctadecanoate*				
30	8.24	0.536	25.1	17.6 ± 0.1[b]
	8.39	0.737	44.9	16.2 ± 0.1
	8.21	0.837	59.8	14.1 ± 0.1
	8.39	0.888	69.8	13.9 ± 0.1
	8.41	0.950	84.8	18.1 ± 0.1
20	16.2	0.165	5.4	2.27 ± 0.03
25	16.5			4.71 ± 0.03
30	16.9			8.63 ± 0.04
35	16.4			15.8 ± 0.1
30	5.33	0.165	5.4	8.17 ± 0.05
	7.94			7.90 ± 0.06
	10.3			8.20 ± 0.05
	20.1			8.00 ± 0.07
erythro-*9(10)-Chloro-10(9)-hydroxyoctadecanoate*				
20	5.82	0.165	5.4	7.49 ± 0.05
25	6.00			14.1 ± 0.2
30	6.09			24.6 ± 0.4
35	6.09			41.9 ± 0.5
25	3.34	0.165	5.4	3.93 ± 0.03
	9.95			14.3 ± 0.1
	12.5			14.4 ± 0.2

[a] ± 0.1°C. [b] Standard error.

Table 2. Rate coefficients of the alkaline dehydrochlorination of sodium *threo-* and *erythro-*9(10)-chloro-10(9)-hydroxyoctadecanoates in water.

Temp.[a] °C	10^2 [OH^-] mol kg^{-1}	10^2 k_{app} kg mol^{-1} s^{-1}	kg mol^{-1} s^{-1}
threo-*9(10)-Chloro-10(9)-hydroxyoctadecanoate*			
	3.94	0.953 ± 0.01[b]	$10^6k_{H_2O}$ = 3.96 ± 1.57
15	8.39	0.727 ± 0.008	10^3k_{OH} = 4.20 ± 1.11
	9.89	0.613 ± 0.006	
	2.06	2.40 ± 0.03	$10^6k_{H_2O}$ = 6.04 ± 0.51
20	4.04	1.50 ± 0.04	10^3k_{OH} = 7.11 ± 0.52
	8.24	1.13 ± 0.01	
	2.17	3.09 ± 0.05	$10^6k_{H_2O}$ = 6.52 ± 0.33
25	4.04	2.25 ± 0.04	10^3k_{OH} = 13.8 ± 0.4
	8.20	1.83 ± 0.02	
	3.83	3.75 ± 0.04	$10^6k_{H_2O}$ = 9.28 ± 1.04
30	5.90	3.35 ± 0.03	10^3k_{OH} = 24.3 ± 0.9
	8.23	3.05 ± 0.04	
35	8.20	4.24 ± 0.05	
erythro-*9(10)-Chloro-10(9)-hydroxyoctadecanoate*			
	1.99	3.15 ± 0.02	$10^6k_{H_2O}$ = 7.91 ± 1.73
15	3.95	2.37 ± 0.03	10^3k_{OH} = 11.1 ± 2.1
	6.81	1.72 ± 0.03	
	2.03	4.51 ± 0.06	
	2.13	4.34 ± 0.09	$10^6k_{H_2O}$ = 10.1 ± 0.6
20	3.75	3.07 ± 0.06	
	5.98	2.72 ± 0.10	
	7.52	2.42 ± 0.04	10^3k_{OH} = 17.0 ± 0.5
	9.93	2.26 ± 0.06	
	2.03	6.68 ± 0.06	
25	2.94	5.47 ± 0.05	$10^6k_{H_2O}$ = 15.2 ± 0.2
	5.92	4.00 ± 0.13	10^3k_{OH} = 25.7 ± 1.8
	7.81	3.65 ± 0.05	
	2.08	10.1 ± 0.1	$10^6k_{H_2O}$ = 18.6 ± 0.5
30	3.11	8.24 ± 0.08	10^3k_{OH} = 49.6 ± 0.8
	4.43	7.30 ± 0.10	

[a] ± 0.1°C. [b] Standard error for 10 – 15 individual values.

Calculation of rate coefficients. The alkaline dehydrochlorinations of the studied *threo* (II) and *erythro* (III) compound follow apparently second-order kinetics.[8] The rate equation is

$$k_{app} = \frac{1}{t(a-b)} \ln \frac{b(a-x)}{a(b-x)} \quad (1)$$

where $a = v_\infty - v_0$ (mequiv./g), $b = [OH^-] - v_0$ (mequiv./g), $[OH^-]$ is the initial hydroxide ion concentration after correction for salt formation with the chlorohydroxy acid, and v_0 is the initial and v_∞ the final consumption of the titrant. The rate coefficients were calculated from the equation

$$k_{app} = \frac{1}{(v_\infty - [OH^-])(t - t_0)} \ln \frac{([OH^-] - v_0)(v_\infty - v_t)}{(v_\infty - v_0)([OH^-] - v_t)} \quad (2)$$

where t_0 is the time of removal of the first sample and v_t the consumption of the titrant (mequiv./g) at time t.

The second-order rate coefficients (k_{OH}) for the dehydrochlorinations in aqueous ethylene glycol mixtures were obtained directly from eqn. (2), but only apparent second-order rate coefficients of the reactions in water were obtained from this equation. The following expression may be written for the rates of the reactions in alkaline water solutions:[9]

$$k_{app}[OH^-][S] = (k_0 + k_{OH}[OH^-])[S] \quad (3)$$

k_{app} is the observed second-order rate coefficient (eqn. (2)), [S] the substrate concentration, and k_0 the rate coefficient of the reaction catalyzed by water. The apparent second-

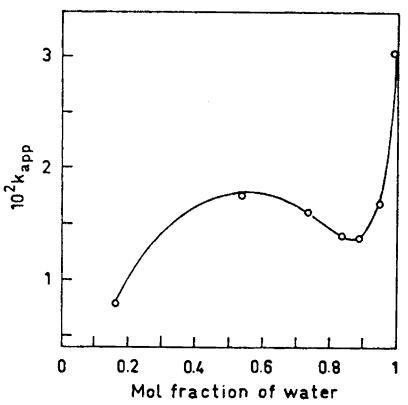


Fig.1. Dependence of the observed second-order rate coefficient (k_{app}) of the alkaline dehydrochlorination of sodium *threo*-9(10)-chloro-10(9)-hydroxyoctadecanoate on water content in aqueous ethylene glycol mixtures at 30°C.

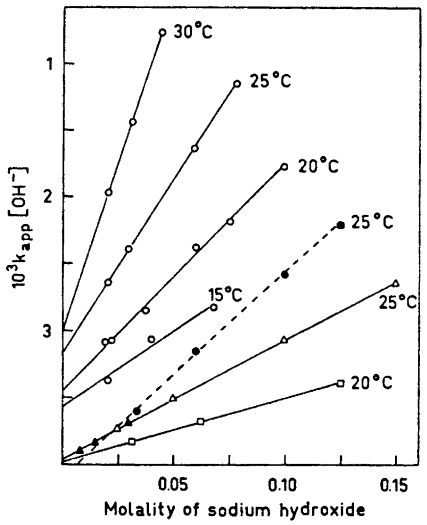


Fig. 2. First-order rate coefficient $k_{app}[OH^-]$ of dehydrochlorination of sodium *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoate (A) and ethylene chlorohydrin (B) as a function of hydroxide ion concentration in water at different temperatures. A. ○, this work. ●, this work: aqueous ethylene glycol mixture ($x_{H_2O} = 0.165$). B. ▲, values of Smith.[20] △, values of Ballinger and Long.[22] □, values of Porret.[21]

order kinetics of the neutral reaction is due to the fact that each released mol of hydrogen chloride consumes one mol of sodium hydroxide. Consequently, the relation

$$k_{app}[OH^-] = k_0 + k_{OH}[OH^-] \quad (4)$$

represents a straight line whose slope is equal to k_{OH} and intercept to k_0. The values of these quantities were determined by the method of least squares (Fig. 2 and Tables 2 and 3).

Table 3. Values of thermodynamic functions of activation at 25°C for the alkaline dehydrochlorination of sodium *threo-* and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoates in water and in an aqueous ethylene glycol mixture ($x_{H_2O} = 0.165$).

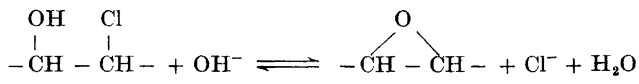
Compound [a]		$\Delta H^{\ddagger}$ kJ mol^{-1}	$\Delta S^{\ddagger}$ J deg^{-1} mol^{-1}	$\Delta G^{\ddagger}$ kJ mol^{-1}	Ref.
In water					
I[b]	A	78.0 ± 3.9[c]	−19.5 ± 13.1[c]	83.8 ± 0.09[c]	This work
I[b]	B	35.8 ± 6.5	−223.6 ± 21.9	102.4 ± 0.14	This work
II	A	68.6 ± 6.7	−44.4 ± 22.5	81.8 ± 0.14	This work
II	B	40.7 ± 3.9	−201.2 ± 13.2	100.7 ± 0.09	This work
III[d]		90.8 ± 0.9	+20.5 ± 2.1	84.5 ± 0.05	(21)
III[d]		81.6 ± 3.4	−9.6 ± 10.0	84.5 ± 0.13	(10)
III[d]		95.0 ± 0.5	+35.2 ± 1.3	84.5 ± 0.02	(25)
III[d,e]		103.8 ± 3.8	−102.1 ± 10.9	134.3 ± 0.54	(24)
III	A[f]	88.3	+12.1	84.7	(20,21,22)
III	B[f]	71.4	−123.8	108.4	(20,21,22)
In aqueous ethylene glycol					
I		94.2 ± 2.4	+26.1 ± 8.0	86.4 ± 0.05	This work
II		83.5 ± 1.6	−0.4 ± 5.3	83.6 ± 0.04	This work

[a] I, sodium *threo*-9(10)-chloro-10(9)-hydroxyoctadecanoate; II, sodium *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoate; III, ethylene chlorohydrin. [b] A, base catalyzed reaction; B, water reaction. [c] Standard deviation. [d] Over-all reaction. [e] Neutral hydrolysis. [f] Recalculated from literature values.

RESULTS AND DISCUSSION

Solvent effects. The rates of the dehydrochlorination of the *threo* and *erythro* compounds depend greatly on the composition of the ethylene glycol-water mixture (see Fig. 1 and Tables 1, 2, and 3). Stevens *et al.*[8] investigated the alkaline dehydrochlorination of ethylene chlorohydrin in alcohol-water and dioxane-water mixtures. Their results are not, however, directly comparable with the results obtained in this work owing to the different solvent mixtures. The solvent effects on alkaline dehydrochlorination reaction were extensively discussed in an earlier paper.[1c]

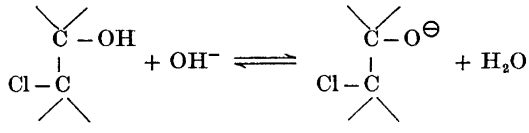
Mechanism of dehydrochlorination. After the study of Evans [10] in the year 1891 the kinetics and mechanism of the reaction between hydroxide ion and ethylene chlorohydrin have been the subjects of several investigations.[11–13] This reaction is subject to specific rather than to general base catalysis.[13]



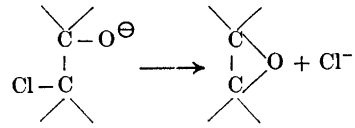
(5)

The reverse reaction does not play any significant role [14] and the effect of ionic strength on the reaction rate is very small except when the ionic strength is high.[15] The main product in alkaline media is the epoxide.[8] Reactions of various halogenohydroxyoactadecanoates in alkaline media have also been described by many authors,[3–5] but the kinetics and mechanisms of the reactions have not been clarified.

According to Winstein and Lucas [11] the reaction mechanism is the following:



(6)



(7)

The reaction involves a pre-equilibrium stage (eqn. (6)) followed by the rate-determining release of the chloride ions (eqn. (7)). This mechanism was later confirmed by the experiments of Swain *et al.*[12]

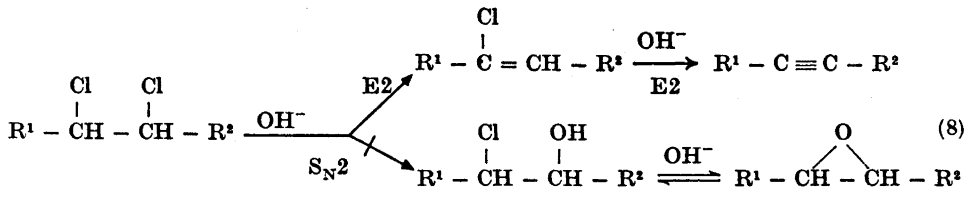
The mechanisms of the alkaline dehydrochlorination reactions of II and III in water and in aqueous ethylene glycol mixtures were in agreement with NMR analyses of the reaction products. The *threo*- and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoic acids give characteristic signals at 3.40 – 3.95 ppm and 3.59 – 4.04 ppm, respectively, from TMS that indicate the presence of the secondary –C*H*OH– grouping (lit. 3.4 – 3.6 ppm;[16,17] 3.3 – 3.7 ppm [18]) and the –C*H*Cl– grouping (lit. 3.8 – 4.3 ppm;[18] 4.0 – 4.3 ppm [19]). After treatment of the acids with alkali in water and in aqueous ethylene glycol, the above signals were replaced by new ones at 2.81 ppm (II) and 2.46 ppm (III). The ring protons of *cis*-9,10-epoxy- and *trans*-9,10-epoxyoctadecanoic acids resonate at 2.80 and 2.46 ppm, respectively, in close agreement with the above values.[17] The fact that the presence of a secondary –CHOH– grouping could not be verified supports the conclusion that the main products are epoxy acids. These observations are in good agreement with the results obtained with ethylene chlorohydrin by Stevens *et al.*[8] The present results confirm the alkaline dehydrochlorination of II and III to occur by the same mechanism as that of ethylene chlorohydrin (eqns. (5) – (7)).

Water reaction. There are many contradictory observations on the alkaline dehydrochlorination of ethylene chlorohydrin, *e.g.*, on the dependence of the reaction rate on the initial concentrations of the reactants.[20–22] According to Winstrom and Warner,[15] this may be due to the effect of carbon dioxide on the alkaline reagent. Ballinger and Long [22] assumed that the dependence is mainly due to a primary salt effect, although, according to earlier reports, the primary salt effect is negligible.[15,20] Our results showed that the second-order rate coefficients increase with decreasing base concentration and that the first-order rate coefficients ($k_{app}[OH^-]$) of II and III vary linearly as the concentration of the base in aqueous ethylene glycol mixtures and in water (Fig.

2; Tables 1 and 2). Only the base catalysis could be detected in the mixtures, whereas in water the neutral reaction contributes appreciably to the rate as seen in Fig. 2 and Table 2. The reaction of ethylene chlorohydrin with water has earlier been found to be very slow [15] and has consequently been disregarded in examinations of the rates of dehydrochlorination of this compound. The present results led, however, to the conclusion that the contribution of the water reaction in alkaline water solution is significant and may even be augmented by substitution. The *threo* and *erythro* acids II and III may be considered disubstituted ethylene chlorohydrins. The great increase in reaction rate with increasing water content of the solvent (Fig. 1) seems to be due to a significant contribution of the water reaction. Using literature values [20–22] for ethylene chlorohydrin in alkaline water solution and plotting $k_{app}[OH^-]$ as a function of base concentration (Fig. 2), it was possible to estimate the second-order rate coefficient of the water reaction (k_{H_2O}) of this compound. Values of the rate coefficient $k_0/55.5 = k_{H_2O}$ (M^{-1} s^{-1}) calculated in the way are 6.5×10^{-7} at 25° and 2.2×10^{-7} at 20°C and values of the rate coefficient of the base-catalyzed reaction k_{OH} (M^{-1} s^{-1}) 8.9×10^{-3} at 25° and 4.8×10^{-3} at 20°C.[20–22] These values are very reasonable when compared with those for II and III (Table 2). The values of k_{H_2O} and k_{OH} for ethylene chlorohydrin, II and III show that alkyl-substitution increases the over-all reaction rate as reported earlier [13,23] and increases the rate of the water reaction appreciably more than that of the reaction catalyzed by hydroxide ion.

The activation enthalpy is greater for the water reaction than for the base-catalyzed reaction (Table 3). The ratio $k_{H_2O}/k^0_{H_2O}$, where k_{H_2O} is the second-order rate coefficient of the water reaction in alkaline water [20,22] and $k^0_{H_2O}$ the second-order rate coefficient of the neutral hydrolysis,[24] is of the order of 10^4 for ethylene chlorohydrin at 25°C. We can see from Table 3 that the value of the free energy of activation for the latter reaction of ethylene chlorohydrin is markedly larger than that for the water reaction, 134 and 108 kJ per mol, respectively, These values led us to conclude that the mechanism of the water reaction in alkaline media differs somewhat from that of the neutral hydrolysis in water. The results of analyses of the reaction products of II and III are in agreement with this conclusion. According to Cowan *et al.*,[24] glycol is the main product in the neutral hydrolysis of ethylene chlorohydrin in water. In this work no alkoxy or hydroxyl groups were detected in the products formed in alkaline aqueous ethylene glycol or in water, whereas epoxide formation was observed in both cases. The water-catalyzed reaction of ethylene chlorohydrin in water containing hydroxide ions requires, however, more detailed supplementary studies because the contribution of the reaction to the over-all rate of dehydrochlorination is very much smaller than in the case of the salts of long-chain chlorohydroxy acids studies in the present work.

Final choice between the possible routes of the alkaline dehydrochlorination of sodium threo-*9,10-dichloro-octadecanoate.* As reported earlier,[1b,1c] the alkaline dehydrochlorination of sodium *threo*-9,10-dichlorooctadecanoate (I) may occur by bimolecular substitution or elimination:



$R^1 = CH_3(CH_2)_7-$
$R^2 = -(CH_2)_7COONa$

The relative rates of the first and second stages of dehydrochlorination of I and the relative rate of dehydrochlorination of II in aqueous ethylene glycol ($x_{H_2O} = 0.165$) at 90°C are 1, 0.003, and 15 000, respectively. The very high rate of reaction of II in comparison with that of the second stage of dehydrochlorination of I supports the view that substitution occurs to only a negligible extent. The same situation prevails also in the alkaline dehydrochlorination of sodium *threo,threo*-9,10,12,13-tetrachlorooctadecanoate.[1d] Almost equal amounts of chlorine were observed to be removed in both stages of dehydrochlorination of I. Consequently, the above and earlier results [1b,1c] show that the S_N2 mechanism (eqn. (8)) may be disregarded in the alkaline dehydrochlorination of I in aqueous ethylene glycol mixtures.

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