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Chlorinated Long-chain Fatty Acids. Their Properties and Reactions. VIII. The Kinetics and Stereochemistry of the Alkaline Dehydrochlorination of Diastereoisomeric Sodium 9,10-Dichlorooctadecanoates

KALEVI PIHLAJA* and MARTTI KETOLA

Department of Chemistry, University of Turku, SF-20500 Turku 50, Finland

The base-promoted removal of the first chlorine of sodium *erythro*-9,10-dichlorooctadecanoate in aqueous ethylene glycol was found to produce sodium 9(10)-chloro-*cis*-octadecenoate. The corresponding *threo* isomer gave 9(10)-chloro-*trans*-9-octadecenoate by a 2.5 times higher rate (363 K) in identical circumstances.

When kept in aqueous alkaline ethylene glycol (5.4 wt. % of water) at 418 K *threo*-dichloride lost all of its chlorine within 24 h, whereas *erythro*-dichloride lost only 68 % of its chlorine content within 825 h in agreement with the fact that intermediate vinylic *cis*-monochlorides react much slower than the corresponding *trans*-monochlorides.

Stereochemically the first reaction step is a *trans*-elimination process in which the different reaction rates of the diastereoisomers were shown to be mainly due to the differences in the ground state energies of their reactive conformations [$k_{threo}/k_{erythro} = 5.0$ (obs.) and 6.5 (calc.) at 298 K].

Diastereoisomeric compounds, such as *threo*- and *erythro*-isomers, may have different reaction rates.[1] For example, the base-promoted dehydrochlorinations of sodium *threo*- and *erythro*-9(10)-chloro-10(9)-hydroxyoctadecanoates have been found to occur at different rates.[2]

The kinetics and mechanisms of the removal of HCl from sodium *threo*-9,10-dichlorooctadecanoate have been studied earlier.[3,4] To complete these studies and to clarify the stereochemical course of the reaction, sodium *erythro*-9,10-dichlorooctadecanoate (*1*) was also prepared and subjected to alkaline dehydrochlorination.

EXPERIMENTAL

GLC analyses were carried out on a Perkin Elmer F 11 gas chromatograph equipped with a hydrogen flame ionization detector. The stainless steel columns were packed with Chromosorb G (60/80 mesh) coated with a polar (5 % XE-60, 200 cm × 3 mm) or non-polar silicone grease (3 % SE-30, 300 cm × 3 mm). The chromatograms were run under isothermal conditions at 160 °C with the former column and at 210 °C with the latter. Before analyses the acids were esterified with diazomethane in diethyl ether containing 10 % of methanol (v/v). The methyl esters of stearic (C18), arachidic (C20), 9-octadecynoic (C18) and 9(10)-chloro-*trans*-9-octadecenoic acids were used as reference compounds.

Proton resonance spectra were recorded on a Perkin Elmer R10 spectrometer (60 MHz) using CCl_4 as solvent and tetramethyl silane (TMS) as internal reference. The sample concentrations varied from 5 to 10 % (w/w). A Perkin Elmer Model 180 spectrophotometer was used to record IR absorption spectra using a thin film of sample between KBr windows. UV absorption spectra were run on a Unicam SP 800 spectrophotometer using absolute ethanol (the State Alcohol Monopoly, Grade AaS, for Spectrophotometry) as solvent. Mass spectra of the prepared methyl esters of the acids were determined with GLC-MS [0.9 m × 3 mm stainless steel column filled with silicone oil OV-17 (2 %; on Chromosorb G 60/80 mesh; 220 °C) connected to a Perkin Elmer M 270 mass spectrometer (ionizing potential 70 eV)].

The chlorine contents of *erythro*-9,10-dichlorooctadecanoic acid and its dehydrochlorination products were determined by the method described previously.[5]

Kinetic measurements and calculation of the reaction rate coefficients were accomplished as shown earlier.[3,4]

Syntheses. Elaidic acid was prepared by isomerization of oleic acid (Fluka AG, 96 % by GLC) by nitrogen oxide.[6] Its melting point after consecutive recrystallizations from diethyl ether and acetone at −17 °C was 42.5 °C (lit.[6] 43−44 °C).

erythro-9,10-Dichlorooctadecanoic acid was obtained by chlorination of elaidic acid (12 g) in CCl_4 solution (150 ml) saturated with chlorine.[5] After evaporation of solvent and excess chlorine the oily residue was treated with urea (12 g) in 100 ml of chloroform containing 10 ml of methanol to remove saturated acids present as impurities in the starting material. The mixture was stirred at 22 °C for 44 h. The excess urea and its fatty acid complexes were then filtered off. Recrystallization of the crude dichloride (about 17 g, after removal of solvent) twice from hexane (4 g of acid per 1 ml of solvent) at −17 °C yielded 7.2 g of acid, m.p. 44.5−45.5 °C (lit.[7] 47.5 °C). The chlorine content based on six determinations was 20.39±0.11 % (calc. 20.07 %). ^{1}H NMR (CCl_4): δ 0.89 (CH_3-), 1.33 [$-(CH_2)_n-$], 2.22−2.31 ($-CH_2COOH$), 1.86 ($-CH_2CHCl-$), 3.9 [$-CH(Cl)-$], and 12.1 ($COOH$). IR, ν_{max}: 1710 (COOH) and 646 cm^{-1} (C−Cl). The acid was converted to its sodium salt (*1*) by methanolic alkali.

Separation of the reaction products. The products formed in the first dehydrochlorination step were obtained by keeping a sample of sodium *erythro*-9,10-dichlorooctadecanoate (*1*) in aqueous alkaline ethylene glycol at 110 °C for 100 min. For the further removal of HCl from the vinylic monochloride formed from *1* more drastic conditions were used: the reaction vessel was kept at 145 °C for 343 and 825 h. The reaction mixture included 1.5 g of *1* and 0.3 mol of NaOH in 400 g of ethylene glycol, which contained 5.4 % of water by weight. The dehydrochlorination products were separated from the reaction mixtures by extraction with CCl_4 as described in an earlier paper.[8] The amount of the viscous residues was about 1 g in each case.

RESULTS AND DISCUSSION

Analyses of the reaction products. After esterification with diazomethane the dehydrochlorination products of *1* separated from the reaction mixtures were analyzed by GLC, NMR, IR, UV, and mass spectroscopy.

The product, after the first dehydrochlorination step, contained 10.1 % of chlorine (10.0 % in theory). IR ν_{max}: 3030 (CH=), 1710 (COOH), 1650 (CH=CCl) and 650 cm^{-1} (C−Cl), ^{1}H NMR (CCl_4): δ 0.89 (CH_3-), 1.96 ($-CH_2CH=$), 2.08 ($-CH_2CCl=$ or $-CH_2C=$), and 5.51 ($-CH=CCl-$; a triplet; J=7.5 Hz). The weak signal at about δ 3.6 may be due to $-CH(OR)-$, where R may be H or the anion of ethylene glycol, or to the alkoxy protons of $-CH(OCH_2CH_2OH)=CH-$. These systems may be formed through the addition of water or ethylene glycol to a double or triple bond. The UV spectrum of the first-step product had a maximum at 218 nm and an inflexion at 232 nm, which may be due to the formation of some conjugated dienes.

Because of the low reactivity of vinylic chloride formed in the first dehydrochlorination step of *1* the removal of the second mol of HCl required more vigorous reaction conditions: a sample of *1* was treated with alkaline reagent for 343 and 825 h at 145 °C. The dehydrochlorination products separated contained 8.3 and 6.4 % of chlorine, respectively. The IR spectrum of the product obtained after the shorter dehydrochlorination period had a new band at 1960 cm^{-1} (C=C=C), which is weakened by the prolonged alkali treatment. The product after 825 h showed also a weak IR band at 2280 cm^{-1} (C≡C). The presence of the allene group is confirmed by a multiplet at δ 5.0 in the NMR spectra of the dehydrochlorination products separated after 343 and 825 h. The product after 343 h had UV maxima at 228 and 255 nm, but after 825 h, only at 255 nm.

The GLC data relative to methyl stearate for the 'methylated' dehydrochlorination products of *1* are collected in Table 1. The results show, that on the polar XE-60 column, the main component (peak 2) of the first dehydrochlorination product is eluted after methyl 9(10)-chloro-*trans*-9-octadecenoate (peak 11). On the non-polar SE-30 column these compounds (peaks 2 and 11) have similar relative retention times. These results are in accordance with those of Stein [9] and Gunstone [10] for the corresponding bromo derivatives, methyl 9(10)-bromo-*cis*-9- and 9(10)-bromo-*trans*-9-octadecenoates. The mass spectrum of peak 2 showed the parent peak (M^+) at *m/e* 331 in agreement with the molecular weight (330.9) of $C_{19}H_{35}O_2Cl$ and the fragment peaks at *m/e* 299, 294, and 263, probably due to $[M-CH_3OH]^+$, $[M-HCl]^+$, and $[M-CH_3OH-HCl]^+$, respectively. Thus the principal product

Table 1. Gas chromatographic retention data for some model compounds and for dehydrochlorination products of sodium *erythro*-9,10-dichlorooctadecanoate (*1*). Retention times are given relative to the retention times for methyl stearate [1.00≡5.24 min (XE-60) and 1.00≡ 6.5 min (SE-30)].

Peak No.	Compound	Relative retention times XE-60	SE-30
Methyl esters of the dehydrochlorination products			
110 °C; 100 min			
1		0.97	0.86
			1.01
			1.18
2		2.56[a]	1.60[a]
145 °C; 343 h			
3		1.11	
4		1.21	1.00
2		2.56[a]	1.63[a]
145 °C; 825 h			
3		1.09	
4		1.21	1.01
2		2.52[a]	1.63[a]
Methyl esters of model acids			
5	Alkali-conjugated linoleic acid	1.01	0.93
6		1.36[a]	1.05[a]
7		1.53	1.18
8	Stearic acid	1.00	1.00
9	9-Octadecynoic (stearolic) acid	1.21	1.00
10	Arachidic acid (C20)	2.26	1.91
11	9(10)-Chloro-*trans*-9-octadecenoic acid	2.36	1.61

[a] The major peak in the chromatogram.

in the first dehydrochlorination step seems to be sodium 9(10)-chloro-*cis*-9-octadecenoate.

Two compounds formed after the further dehydrochlorination (peaks 3 and 4 in Table 1) gave the molecular ion peaks at *m/e* 294 indicating the presence of dienic, allenic, or ynoic esters with the molecular weight (294.4) of $C_{19}H_{34}O_2$. According to the GLC data peak 4 may be an acetylenic ester since its relative retention time on the XE-60 column is equal to that of an authentic sample of methyl 9-octadecynoate (peak 9). Gunstone *et al.*[10] observed that on a polar column the long-chain allenic C_{18}-ester was eluted before the corresponding acetylenic one. Thus the relative retention times 1.1 (peak 3) and 1.2 (peak 4) may also indicate that the former is an allenic intermediate. Moreover, after 343 h the area of the peak of the allenic ester (peak 3 in Table 1) was larger than that of the ynoic ester (peak 4), while after the dehydrochlorination for 825 h, the order was reversed.

GLC and UV spectroscopy pointed out that the first-step dehydrochlorination product contained only small amounts of conjugated dienes, which moreover, were not among the products formed during the further dehydrochlorination of *1*. In the latter case the equilibrium reached was in favour of allenes and acetylenes, but not of conjugated dienes (Scheme 1).

Kinetics and mechanisms of dehydrochlorination. The values of the rate coefficients at five temperatures are collected in Table 2 and the values of thermodynamic functions of activation obtained from them by the method of least squares, in Table 3. Accordingly, the first chlorine from sodium *erythro*-9,10-dichlorooctadecanoate (*1*) is removed as HCl rather easily, although the rate of this reaction is about 2.5 times higher for the corresponding *threo* isomer under identical conditions (Table 3). This observation is in accordance with that reported by Gunstone *et al.*[10] for the corresponding dibromooctadecanoates. The removal of HCl from the vinylic *cis*-monochloride under the conditions used was too slow for determination. By heating of *1* with alkali for 825 h at 145 °C 36 % of the second chlorine was reacted,

Table 2. Rate coefficients for the first dehydrochlorination step of sodium *erythro*-9,10-dichlorooctadecanoate in aqueous alkaline ethylene glycol ($x_{H_2O}=0.165$) at different temperatures.[a]

Temperature °C	10^5k (s^{-1})	10^5k_{OH} (kg mol^{-1} s^{-1})
80	7.02 ± 0.09[b]	4.54 ± 0.06[b]
90	20.5 ± 0.3	13.3 ± 0.2
90	19.9 ± 0.3	12.9 ± 0.2
95	32.4 ± 0.3	20.5 ± 0.2
100	51.0 ± 0.6	33.0 ± 0.4
100	48.0 ± 0.6	31.1 ± 0.4

[a] The substrate concentration was 0.01 mol per kg of solvent, sodium hydroxide concentration was 0.773 mol per kg of solvent. [b] Standard deviation.

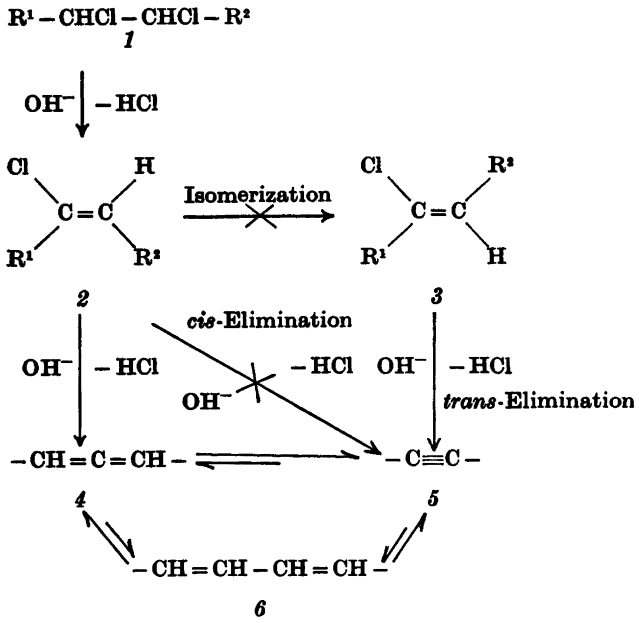
Table 3. Values of the thermodynamic functions of activation and relative rates at 90 °C for the alkaline dehydrochlorination of sodium *threo*- and *erythro*-9,10-dichlorooctadecanoates in aqueous alkaline ethylene glycol containing 16.5 mol % of water.

	Reaction step	$\Delta H^{\ddagger}$ kJ mol^{-1}	$\Delta S^{\ddagger}$ J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$ kJ mol^{-1}	Rel. rate
erythro	I	103.2 ± 2.4[a]	-36.9 ± 6.6[a]	116.6 ± 0.05[a]	140
threo [b]	I	93.8 ± 0.4	-55.3 ± 1.2	113.9 ± 0.02	340
	II	108.1 ± 1.8	-64.3 ± 4.3	131.5 ± 0.2	1

[a] Standard deviation. [b] Refs. 3, 4.

whereas from *threo*-9,10-dichlorooctadecanoate all chlorines were removed after 24 h at 145 °C. This result confirms that the dehydrochlorination of *1* also occurs through *trans*(*anti*)-elimination (E2) where 9(10)-chloro-*cis*-9-octadecenoate is the first step product. The difficulty of the further dehydrochlorination of this *cis*-monochloro-ene (*2*) is mainly due to the great steric hindrance for the *cis*-(*syn*)-elimination.

According to Staley and Doherty [11] the formation of allene from 4-bromo-*cis*-4-octene is very much faster than that of the triple bond through *cis*(*syn*)-elimination. Their results show also that *trans*(*anti*)-elimination of HBr from 4-bromo-*trans*-4-octene yields the triple bond about forty times faster than the corresponding *cis*-isomer forms the allene. Thus the rates of dehydrobromination of monobromooctenes decrease in the sequence $k_{anti} > k_{allene} > k_{syn}$. Vigorous treatment of *1* with alkali yielded acetylenic and allenic intermediates but very little, or no conjugated dienes in accordance with the above results and those of Gunstone



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

Scheme 1. The possible reaction pathways in the alkaline dehydrochlorination of *1*.

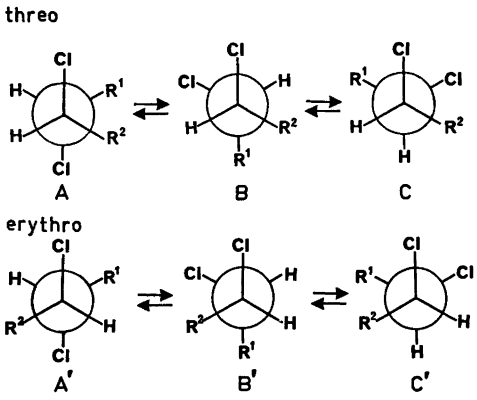


Fig. 1. The minimum energy conformations of sodium *threo*-(A – C) and *erythro*-9,10-dichlorooctadecanoates (A′ – C′).

et al.[10] for the corresponding bromo octadecanoates. Consequently, the base-promoted dehydrochlorination of *1* may be proposed to occur through the following steps (Scheme 1): in the first reaction step *trans*(*anti*)-elimination produces 9(10)-chloro-*cis*-9-octadecenoate (*2*) which during prolonged dehydrochlorination gives allenic intermediates (*4*) and octadecynoates (*5*) both of which are in equilibrium with dienic derivatives (*6*). The formation of *5* through *cis*(*syn*)-elimination or through isomerisation of *2* to *trans*-chloro-ene (*3*) followed by *trans* (*anti*)-elimination is only of minor importance. Secondary isomerizations of *4* and *5* may, of course, give other allenic and acetylenic derivatives,[12,13] which may also be formed from the vinylic *cis*-chloro alkene *2* (Scheme 1) through elimination of HCl preceded by a double bond shift.

Stereochemistry of the first dehydrochlorination step. The basepromoted dehydrochlorination proceeds under the conditions used by E2 mechanism.[14] A stereochemical requirement for this mechanism is that the leaving groups H and Cl are in an *anti* (or *trans*) periplanar conformation.[3,4,14,15]

Both sodium *threo*- and sodium *erythro*-9,10-dichlorooctadecanoates have three minimum energy conformations (Fig. 1) from which only C (*threo* isomer) and B′ and C′ (*erythro* isomer) can undergo the E2 elimination.

The rate of a given reaction of a conformationally heterogeneous system may be presented by the relation [15]

$$k = \sum x_i k_i$$

where x_i is the mol fraction and k_i the rate coefficient of the reaction studied for the ith conformation. Hence the total rates for the first dehydrochlorination steps of sodium *threo* (k_t) and *erythro*-9,10-dichlorooctadecanoates (k_e) may be written

$$k_t = k_A x_A + k_B x_B + k_C x_C$$

$$k_e = k_{A'} x_{A'} + k_{B'} x_{B'} + k_{C'} x_{C'}$$

If the dehydrochlorination reaction occurs predominantly as an *anti*-elimination $k_C \gg k_A \approx k_B \approx 0$ and $k_{C'} \approx k_{B'} \gg k_{A'} \approx 0$. Accordingly,

$$k_t \approx k_C x_C \text{ and}$$

$$k_e = k_{B'} x_{B'} + k_{C'} x_{C'}$$

Moreover, it is reasonable to assume that $k_C = 2k_{B'} = 2k_{C'}$ and $x_{B'} = x_{C'}$ where the factor two is due to the double *anti*-arrangement of the conformation C.[14] Consequently,

$$k_t/k_e = x_C/x_{C'}$$

If the *gauche* interactions due to the groupings R^1 and R^2 do not differ essentially from those of a methyl group the mol fraction of the different conformations may be estimated using the following values (in kJ mol^{-1}) for the various *gauche* interactions at 298 K: $R^1 - R^2$ (Me – Me) [16] + 2.7, Cl – Cl [17] + 5.0, and R^1 – Cl or R^2 – Cl (Me – Cl) [17] – 0.2.

The estimated interaction energies for the conformations of *threo*- and *erythro*-9,10-dichlorooctadecanoates are then (Fig. 1)

A + 2.3	B + 7.7	C + 4.6
A′ – 0.4	B′ + 7.5	C′ + 7.5

Since [15] $x_i/x_{i+1} = \exp\ [(H_i - H_{i+1})/RT]$ and $\sum x_i = 1$ we can estimate that $x_C \simeq 0.26$ and $x_{C'} = 0.04$ and thus $k_t/k_e \simeq x_C/x_{C'} \simeq 6.5$ at 298 K. Experimentally, the rate ratio for the *threo*- and *erythro*-9,10-dichlorooctadecanoates was found to be 2.5 at 363 K and 5.0 at 298 K.[14]

The calculated and experimental results being very close to each other support the postulation that the reaction is really preponderantly *trans*-elimination (E2) and that the difference in the reaction rates is mainly due to the different ground state energies of the reactive conformations of the *threo* and *erythro* isomers.

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