Kinetics of the Hydrolysis of α-Halo-*sec.*-alkyl Esters in Acetone-Water Mixtures*

ERKKI K. EURANTO

Department of Chemistry, University of Turku, Turku, Finland

The kinetics of the hydrolysis of several α-halo-*sec.*-alkyl esters R'COOCXR''R''', in which R' is CH₃, C₂H₅, or CCl₃, R'' and R''' are alkyl groups, and X is Cl or Br, and of α-chloroethyl acetate in acetone-water mixtures at several temperatures has been investigated by a conductometric or an argentometric method. The mechanisms of the reactions are unimolecular substitutions of halogen (S_N1) except in the case of α-chloroisopropyl trichloroacetate, where the reaction is neutral ester hydrolysis ($B_{AC}2$). The rates of the S_N1 reactions of the α-halo-*sec.*-alkyl esters are more than a thousand times those of the corresponding α-haloethyl esters in the same conditions. The solvent composition has a very similar influence in both cases. The bromoesters studied react about 26 times as fast as the corresponding chloroesters. The inductive effect determines the relative rate when the structure of the acyl component or the substituent in the γ-position of the alkyl component of the ester is varied, but if a β-hydrogen atom is substituted by an alkyl group, the Baker-Nathan order is followed. α-Chlorocyclohexyl acetate reacts at about one tenth of the rate of diethylchloromethyl acetate; this retarding effect, due to a change in activation enthalpy, is typical of solvolytic reactions of cyclohexyl compounds (*I* strain).

The hydrolyses of α-chloroethyl acetate[2] and other α-haloethyl esters[3] have been previously found to take place as a solvolysis of halogen by the S_N1 mechanism, and their rates were found to be about one thousand times the rates of the corresponding halomethyl esters. The only α-halo-*sec.*-alkyl esters that have been investigated kinetically earlier are α,β-dichloroisopropyl acetate and butyrate and α,β,β'-trichloroisopropyl acetate.[4] Attempts to prepare α-halo-*sec.*-alkyl esters without other electronegative substituents by customary methods were unsuccessful,[5] but a slightly modified method[6,7] proved feasible and several of these esters were prepared.[7] A kinetic study of the hydrolysis of these esters has now been carried out and the results are reported in this paper together with some new data for α-chloroethyl acetate.

---

* A preliminary communication[1] was read at the 1966 Meeting of the Finnish Chemical Society in Oulu, Finland, on May 16th, 1966.

EXPERIMENTAL

Materials. The solvent mixtures were prepared by mixing an accurately measured volume of distilled water, purified by passing it through a mixed-bed ion exchanger, and acetone (E. Merck AG, Guaranteed Reagent) in a volumetric flask and filling to the mark with acetone. The symbol p vol. "%" employed in the following means that 100 ml of the solvent mixture contained $(100 - p)$ ml of water. Reaction mixtures containing added salts or hydrogen halides were prepared as described earlier.[2,8]

The syntheses of the α-chloro-*sec.*-alkyl esters have been described earlier.[7,9] The α-bromo-*sec.*-alkyl esters, α-bromoisopropyl acetate [7] and α-bromocyclohexyl acetate, used in the kinetic runs were impure; attempts to isolate the esters from the reaction mixtures were unsuccessful and the preparations contained only a few per cent of the ester.[7] The kinetic results are, however, believed to be reliable, even if inaccurate, because the impurities did not interfere with the conductometric rate measurements seriously owing to their very different rates of reaction.[7]

Kinetic experiments. The rates of reaction were followed in most cases by the conductometric method described earlier.[2,10] The low rates of α-chloroethyl acetate in solutions containing at least 80 vol. "%" acetone and those of α-chloroisopropyl trichloroacetate, however, were measured by an argentometric method described earlier.[2,3]

In general, hydrogen halides and other reaction products had only minor effects on the rates and the calculated first-order rate coefficients k were found to be nearly constant, as seen from the following kinetic data for the hydrolysis of α-chloroisopropyl acetate in 80 vol. "%" acetone-water at 25°C measured by the conductometric method ($\varkappa$, the conductometer reading, is proportional to the specific conductance and x, which is obtained from the calibration curve, is proportional to the concentration of hydrogen chloride):

t (s)	0	5	10	15	20	25	30	40	45	55	65	∞
$\varkappa$	1.98	2.23	2.42	2.59	2.73	2.85	2.95	3.12	3.18	3.28	3.35	3.52
x	9.04	10.45	11.57	12.62	13.51	14.23	14.91	16.10	16.55	17.33	17.90	19.35
10^2k		2.94	2.82	2.84	2.84	2.80	2.81	2.89	2.90	2.96	3.02	

In a few cases, however, the values of the calculated first-order rate coefficients k_t increased significantly with time t because of strong electrolyte effects or acid catalysis (see below). This increase was found to be an almost linear function of the time-average c_t of the hydrogen ion concentration,[2] and a value referring to $c_t = 0$ was extrapolated graphically. This case is illustrated by the data for the hydrolysis of α-chloroisopropyl trichloroacetate in 70 vol. "%" acetone-water at 25°C obtained by the argentometric method:

t (min)	0	40	80	126	180	246	300	400	540	720	∞
V_{AgNO_3} (ml)	0.24	1.53	2.66	3.90	5.17	6.50	7.43	8.89	10.33	11.50	13.09
10^3c_t (M)	0	0.9	3.4	5.8	8.3	11.1	14.2	16.5	20.4	24.8	29.2
10^5k_t (s⁻¹)	4.25	(4.41)	4.35	4.43	4.48	4.52	4.56	4.66	4.75	4.84	

Kinetic data. The means of the first-order rate coefficients together with their standard errors or the values (marked by asterisks) extrapolated to zero hydrogen ion concentration are given in Tables 1, 2, 3, and 5. The values of the activation energy E and the logarithm of the frequency factor A (A in s⁻¹) were calculated by the method of least squares.

DISCUSSION

Neutral ester hydrolysis. The kinetic data for α-chloroisopropyl trichloroacetate deviate clearly from those for the other α-chloroisopropyl esters studied (Table 1). The exceptionally low values of the Arrhenius parameters and the activation enthalpy and entropy (in 80 vol. "%" acetone-water, $\Delta H^{\neq}$ is 8.91 kcal/mole and $\Delta S^{\neq}$ −50.3 E. U.) indicate that the hydrolysis of

α-chloroisopropyl trichloroacetate does not take place as a displacement of chlorine but as a neutral ester hydrolysis by the mechanism $B_{AC}2$ like that of many other esters with electronegative substituents.[2,4,8]

Structural effects in the displacement of chlorine. On comparing the data in Tables 1 and 3 it is seen that the rate coefficients for α-chloroisopropyl acetate are about 1400 times those for α-chloroethyl acetate under the same conditions. Because the reaction of α-chloroethyl acetate is an S_N1 solvolysis of the chlorine atom at least in solvents of high water content,[2] one may conclude that the reaction of α-chloroisopropyl acetate takes place by the same mech-

Table 1. Kinetic data on the hydrolysis of α-chloroisopropyl esters $R'COOCCl(CH_3)_2$ in acetone-water mixtures.

Vol. "%" acetone	R'	t °C	10^3k s^{-1} Mean of a run	Average	log A	E kcal/mole
50	CCl₃*	25	0.177*	0.177		
70	CCl₃*	25	0.0425**			
			0.0427**	0.0426		
80	CCl₃*	25	0.0186**			
			0.0192**	0.0189		
		35	0.0314**			
			0.0317**	0.0316	2.24	9.50
		45	0.0511**		±0.049	±0.069
			0.0525**	0.0518		
	CH₃	25	27.8 ± 0.22			
			28.8 ± 0.23			
			29.0 ± 0.32	28.8		
			29.6 ± 0.24			
	C₂H₅	25	38.0 ± 0.36			
			39.5 ± 0.31	38.8		
85	CCl₃*	25	0.0117**	0.0117		
	CH₃	25	10.2 ± 0.09			
			10.4 ± 0.08			
			10.6 ± 0.08	10.6		
			10.8 ± 0.06			
			10.9 ± 0.06			
	C₂H₅	25	14.6 ± 0.12			
			16.2 ± 0.17	15.4		
90	CCl₃*	25	0.00532**	0.00532		
	CH₃	25	2.72 ± 0.014			
			2.73 ± 0.019	2.72		
		35	7.30 ± 0.031		10.87	18.33
			7.54 ± 0.091	7.50	±0.08	±0.12
			7.66 ± 0.041			
		45	18.3 ± 0.09			
			18.9 ± 0.13	19.0		
			19.8 ± 0.19			
	C₂H₅	25	3.74 ± 0.033			
			3.87 ± 0.069	3.84		
			3.90 ± 0.034			

* Measured by the argentometric method.
** Extrapolated to zero hydrogen chloride concentration.

Table 2. Kinetic data on the hydrolysis of α-halo-*sec.*-alkyl acetates $CH_3COOCXR''R'''$ in acetone-water mixtures.

Vol. "%" acetone	R''	R'''	X	t °C	10^3k s^{-1}		log A	E kcal/mole
					Mean of a run	Average		
70	cycloC$_6$H$_{10}$		Cl	25	4.68 ± 0.017 4.73 ± 0.020	} 4.70		
80	CH$_3$	CH$_3$	Cl	25	See Table 1	28.8		
	CH$_3$	C$_2$H$_5$	Cl	25	22.3 ± 0.13 22.6 ± 0.11	} 22.5		
	CH$_3$	nC$_3$H$_7$	Cl	25	23.5 ± 0.18 24.1 ± 0.22	} 23.8		
	CH$_3$	iC$_3$H$_7$	Cl	25	15.0 ± 0.10 15.2 ± 0.06	} 15.1	} 12.02	18.89
				35	42.1 ± 0.41 42.9 ± 0.42	} 42.5		
	C$_2$H$_5$	C$_2$H$_5$	Cl	25	7.99 ± 0.034 8.35 ± 0.028	} 8.17		
				35	23.2 ± 0.15 23.7 ± 0.15	} 23.4	11.79 ± 0.13	18.93 ± 0.18
				45	60.2 ± 0.48 61.4 ± 0.89	} 60.8		
	cycloC$_6$H$_{10}$		Cl	25	0.866 ± 0.0035 0.868 ± 0.0027	} 0.867		
				35	2.76 ± 0.008 2.79 ± 0.019	} 2.77	12.26 ± 0.13	20.91 ± 0.19
				45	7.88 ± 0.061 8.04 ± 0.039	} 7.96		
85	CH$_3$	CH$_3$	Cl	25	See Table 1	10.6		
	CH$_3$	C$_2$H$_5$	Cl	25	7.90 ± 0.048 8.37 ± 0.048	} 8.14		
	CH$_3$	nC$_3$H$_7$	Cl	25	8.58 ± 0.060 8.70 ± 0.034	} 8.64		
	CH$_3$	iC$_3$H$_7$	Cl	25	5.65 ± 0.040	5.65		
	C$_2$H$_5$	C$_2$H$_5$	Cl	25	3.07 ± 0.020 3.17 ± 0.008	} 3.12		
90	CH$_3$	CH$_3$	Cl	25	See Table 1	2.72	} 10.87 ± 0.08	18.33 ± 0.12
				35		7.50		
				45		19.0		
	CH$_3$	C$_2$H$_5$	Cl	25	2.14 ± 0.025 2.16 ± 0.028	} 2.15		
				35	6.01 ± 0.064 6.04 ± 0.084	} 6.02	10.90 ± 0.13	18.50 ± 0.18
				45	15.2 ± 0.18 15.5 ± 0.25	} 15.3		
	CH$_3$	nC$_3$H$_7$	Cl	25	2.30 ± 0.013 2.36 ± 0.014	} 2.33		
				35	6.43 ± 0.053 6.45 ± 0.065	} 6.44	11.06 ± 0.047	18.68 ± 0.066
				45	16.7 ± 0.15 17.0 ± 0.11	} 16.9		

90	CH₃	iC₃H₇	Cl	25	1.50 ± 0.015 1.54 ± 0.014	1.52		
	C₂H₅	C₂H₅	Cl	25	0.879 ± 0.0059 0.880 ± 0.0069	0.879		
	cycloC₆H₁₀		Cl	25	0.0862±0.00022	0.0862		
	cycloC₆H₁₀		Br	25	2.3 ± 0.15	2.3		
95	CH₃	CH₃	Cl	25	0.292 ± 0.0056 0.302 ± 0.0046	0.297		
	CH₃	CH₃	Br	25	7.50 ± 0.057 7.5 ± 0.23	7.5		

anism. The found large increase in rate is the expected structural effect of the replacement of one α-hydrogen atom by a methyl group (for references, see Ref. 2). The activation energies for these two compounds are almost equal; the rate increase is thus caused by an increase in the activation entropy, the values being −10.8 E.U. for α-chloroisopropyl acetate and −25.5 E.U. for α-chloroethyl acetate in 90 vol. "%" acetone-water. Direct comparison is not possible in other cases but owing to similar structural effects in the series R′COOCHClR″[3] and R′COOCClR″CH₃, the rate coefficients of the members of the last-mentioned series may be concluded to be about 1000 times higher.

The logarithms of the rate coefficients for some α-chloro-sec.-alkyl esters are plotted as functions of the logarithm of the molar water concentration in Fig. 1. The resulting straight lines are seen to be parallel within the limits

Table 3. Kinetic data on the hydrolysis of α-chloroethyl acetate in acetone-water mixtures.

Vol. "%" acetone	t °C	$10^5 k$ s⁻¹		log A	E kcal/mole
		Mean of a run	Average		
50	25	98.2 ± 0.65 98.8 ± 0.25	98.5		
60	25	31.4 ± 0.08 31.8 ± 0.10	31.6		
70	25	9.16 ± 0.028 9.57 ± 0.041	9.36		
80*	25	2.04 ± 0.010 2.08 ± 0.013 2.19 ± 0.024**	2.06		
	35	5.82 ± 0.045	5.82	9.21	18.96
	45	15.4 ± 0.14	15.4	± 0.002	± 0.003
85*	25	0.785 ± 0.0053	0.785		
90*	25	0.189*** 0.39**,***	0.189		
	35	0.515***	0.515	7.65	18.25
	45	1.31***	1.31	± 0.024	± 0.034

   * Measured by the argentometric method.
  ** In a solution obtained by hydrolysing 0.1 M acetyl chloride before the reaction was started.
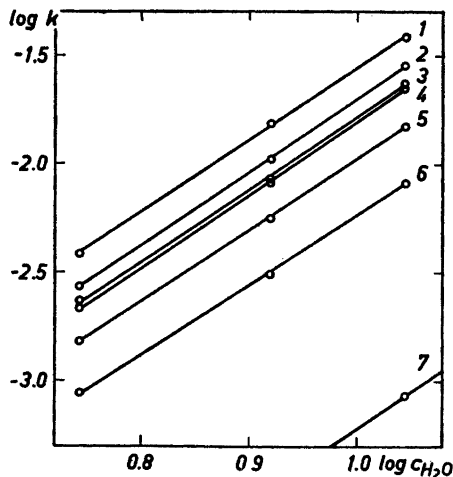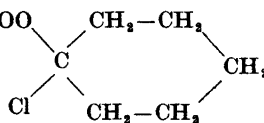 *** Extrapolated to zero or initial** hydrogen chloride concentration.

Fig. 1. The logarithmic dependence of the rate coefficient on the molar water content in the S_N1 hydrolysis of α-chloro-sec.-alkyl esters in acetone-water mixtures at 25°C.

1. $CH_3CH_2COOCCl(CH_3)_2$
2. $CH_3COOCCl(CH_3)_2$
3. $CH_3COOCCl(CH_3)(CH_2CH_2CH_3)$
4. $CH_3COOCCl(CH_3)(C_2H_5)$
5. $CH_3COOCCl(CH_3)(CH(CH_3)_2)$
6. $CH_3COOCCl(C_2H_5)_2$

7.

of experimental error. When considering structural effects one can therefore employ relative rates in any solvent mixture in the range studied. It is seen from Table 1 that when the structure of the acyl component R′ of α-chloro-isopropyl esters R′COOCCl(CH$_3$)$_2$ is varied, electropositive groups increase the rate ($k_{Et}/k_{Me} = 1.4$) and electronegative groups reduce it strongly ($k_{CCl_3}/k_{Me} < 10^{-3}$; the rate of the S_N1 solvolysis of α-chloroisopropyl trichloroacetate is only a small fraction of the observed rate (see above)). These effects are similar to those found for α-chloroethyl esters R′COOCHClCH$_3$ ($k_{Et}/k_{Me} = 1.3$, $k_{CH_2Cl}/k_{Me} = 0.012$).[3]

The rate coefficient diminishes in every case where a β-hydrogen atom of the alkyl component of an α-chloro-sec.-alkyl acetate has been substituted by an alkyl group (Table 4). This is in contrast to the expected influence of the inductive electron release from the electropositive alkyl group. The Baker-Nathan order is thus followed. A contribution of the Baker-Nathan effect is necessary to explain also the structural effects in the hydrolysis of α-chloro-alkyl acetates CH$_3$COOCClR″R‴ with R″ = CH$_2$Cl or H and R‴ = CH$_2$Cl, H, or CH$_3$.[4] These effects will be treated in more detail in a subsequent paper containing additional data. It is to be noted that substitution of a γ-hydrogen

Table 4. Relative rate coefficients of the S_N1 hydrolysis of α-chloroalkyl acetates CH$_3$COOCClR″R‴ in 80−90 vol. "%" acetone-water at 25°C.

R‴ \ R″	H	CH$_3$	C$_2$H$_5$	nC$_3$H$_7$	iC$_3$H$_7$
CH$_3$	0.00072	1	0.78	0.83	0.54
C$_2$H$_5$		0.78	0.30		

atom by a methyl group leads to a slight increase in the rate ($k_{nPr}/k_{Et} = 1.06$, Table 4).

The ratios of the rate coefficients for α-chlorocyclohexyl acetate to those for α-chloroisopropyl acetate and diethylchloromethyl acetate (1-chloro-1-ethylpropyl acetate) are 0.031 and 0.10, respectively (Table 2). Because the electronic effects must be closely similar in the last-mentioned compound and α-chlorocyclohexyl acetate, this difference in rate must be due to a stereochemical influence of the cyclohexyl ring. The effect is similar to that found in the solvolysis of α-methylcyclohexyl chloride,[11] although somewhat more pronounced. Brown [11] has explained it by the aid of I strain, i.e., of "the change in internal strain accompanying a change in coordination number of the ring atom participating in the reaction" (from 4 to 3). The retardation is due to a higher activation energy as in the case of α-methylcyclohexyl chloride.[11]

It is seen from Table 2 that the two α-bromo-sec.-alkyl esters investigated hydrolyse about 26 times as fast as the corresponding chloroesters. This is a slightly smaller ratio than in the case of halomethyl [2] and α-haloethyl [3] esters in solvents of higher water content.

Solvent effects. The effect of water concentration on the rate of solvolysis in the acetone-water mixtures is shown in Figs. 1 and 2. It is seen that the different reaction mechanism of α-chloroisopropyl trichloroacetate becomes evident also as an exceptional variation of the rate with solvent composition. It is possible that the displacement of chlorine begins to compete with neutral ester hydrolysis in the solvents of highest water content.

The plots for the displacement reactions of chlorine are composed of two approximately linear parts, one from water to about 50 vol. "%" acetone-water, the other from about 75 to 95 vol. "%" acetone-water. The slope in the first-mentioned range is about 3.3 for chloromethyl acetate hydrolysing by the S_N2 or an intermediate mechanism [2] and about 5.9 for the S_N1 reaction

Fig. 2. The logarithmic dependence of the rate coefficient on the molar water content in the solvolysis of α-chloroalkyl esters in acetone-water mixtures at 25°C. The data for $CH_3COOCHClCH_3$ are taken partly from Ref. 2, those for $CH_3COOCCl(CH_3)$ (CH_2Cl) from Ref. 4, and those for CH_3COOCH_2Cl from Ref. 2.

1. $CH_3COOCCl(CH_3)_2$

2. CH_3COO, CH_2-CH_2
   C
   Cl CH_2-CH_2 CH_2
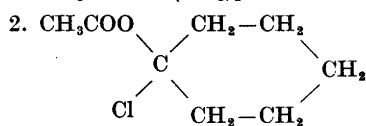
3. $CH_3COOCHClCH_3$
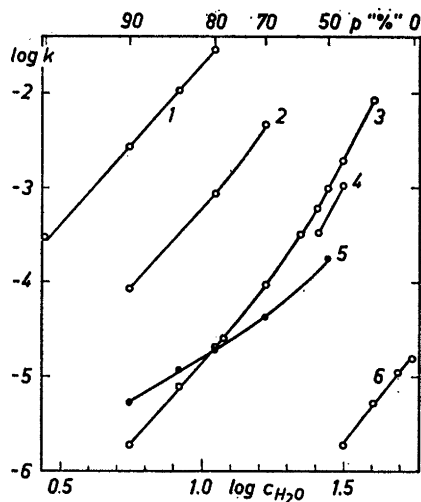4. $CH_3COOCCl(CH_3)(CH_2Cl)$
5. $CCl_3COOCCl(CH_3)_2$
6. CH_3COOCH_2Cl

Table 5. Kinetic data on the hydrolysis of α-chloro-*sec.*-alkyl esters R'COOCClR''R''' in acetone-water mixtures containing added electrolytes at 25°C

Vol. "%" acetone	R'	R''	R'''	Electrolyte	$10^3 k$ s^{-1}
70	CCl₃	CH₃	CH₃*	—	0.0426**
				{ 0.055 M HCl { 0.055 M CCl₃COOH	0.0505**
85	CH₃	CH₃	CH₃	—	10.6
				{ 0.107 M HCl { 0.107 M CH₃COOH	13.3 ± 0.18
				0.05 M NaClO₄	14.1 ± 0.15
				0.10 M NaClO₄	15.8 ± 0.17
				0.05 M NaCl	12.0 ± 0.22
				0.10 M NaCl	13.6 ± 0.28
	CH₃	CH₃	iC₃H₇	—	5.65 ± 0.04
				0.10 M NaClO₄	7.73 ± 0.11
					8.01 ± 0.12
				0.10 M NaCl	6.06 ± 0.05
90	CH₃	CH₃	CH₃	—	2.72
				{ 0.075 M HCl { 0.075 M CH₃COOH	3.21 ± 0.030

* Measured by the argentometric method.
** Extrapolated to initial hydrogen chloride concentration.

of α-chloroethyl acetate.[2] The slope has the same value, 3.4, in the last-mentioned range for α-chloroethyl acetate, α-chloroisopropyl acetate and other α-chloro-*sec.*-alkyl esters. This similarity clearly points to a common mechanism and indicates that the change in the slope at about 60 vol. "%" acetone-water is not due to a change in mechanism, because the reaction mechanism cannot change in the same solvent range in the case of α-chloroethyl acetate and α-chloroisopropyl acetate with an additional α-methyl group and more than a thousandfold rate of solvolysis. A similar change in the apparent order of reaction with respect to water takes place in the solvolysis of *tert.*-butyl bromide in the same range of acetone-water mixtures.[12]

Salt effects. Electrolytes increase the rates of the neutral ester hydrolysis of α-chloroisopropyl trichloroacetate in 70 vol. "%" acetone-water and the solvolyses of α-chloroisopropyl acetate and methylisopropylchloromethyl acetate (1-chloro-1,2-dimethylpropyl acetate) in 85 and 90 vol. "%" acetone-water (Table 5). In the first-mentioned case only the combined effect of the reaction products, hydrogen chloride and trichloroacetic acid, was examined, and it cannot be decided whether the influence is an acid catalysis or an ionic strength effect. The fact that neutral salts diminish the rate of neutral ester hydrolysis of chloromethyl chloroacetate [8] points to the former.

In the case of the solvolyses of other α-chloro-*sec.*-alkyl acetates, 0.1 M sodium perchlorate increases the rate coefficient by 40—50 %, which is of the magnitude often found for the ionic-strength effect in similar solvents.[13] Both hydrogen chloride and sodium chloride also increase the rate, but in a

lesser degree than sodium perchlorate (the rate increase is about 26 % in the case of α-chloroisopropyl acetate but only 7 % in the case of methylisopropyl-chloromethyl acetate). Because the ionic-strength effect does not vary greatly with the nature of the salt,[13] the weaker effect of chlorides is probably due to the common-ion effect and is thus in accordance with the supposed $S_N 1$ mechanism.[2,3]

REFERENCES

1. Euranto, E. K. *Suomen Kemistilehti* **A 39** (1966) 110.
2. Euranto, E. *Ann. Univ. Turku. A I* **1959** No. 31.
3. Euranto, E. *Suomen Kemistilehti* **B 33** (1960) 41.
4. Euranto, E. *Suomen Kemistilehti* **B 35** (1962) 18.
5. Euranto, E. and Kujanpää, T. *Acta Chem. Scand.* **15** (1961) 1209.
6. Imperial Chemical Industries Ltd. *British Patent* 837, 486 (1960).
7. Euranto, E. K. and Leppänen, O. *Acta Chem. Scand.* **17** (1963) 2765.
8. Euranto, E. K. and Cleve, N. J. *Acta Chem. Scand.* **17** (1963) 1584.
9. Euranto, E. K., Noponen, A. and Kujanpää, T. *Acta Chem. Scand.* **20** (1966) 1273.
10. Euranto, E. K. and Leimu, R. S. *Acta Chem. Scand.* **20** (1966) 2028.
11. Brown, H. C., Fletcher, R. S. and Johannesen, R. B. *J. Am. Chem. Soc.* **73** (1951) 212; Brown, H. C. and Borkowski, M. *Ibid.* **74** (1952) 1894.
12. Tommila, E., Tiilikainen, M. and Voipio, A. *Ann. Acad. Sci. Fennicae, Ser. A II* **1955** No. 65.
13. Bateman, L. C., Hughes, E. D. and Ingold, C. K. *J. Chem. Soc.* **1940** 960.