KINETICS OF ACID-CATALYZED HYDROLYSIS OF FLUORINATED PROPANOATES

Oldřich PALETA, Jaroslav KVÍČALA and Václav DĚDEK
Department of Organic Chemistry,
Prague Institute of Chemical Technology, 166 28 Prague 6

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Rates of hydrolysis, k_{H^+}, of methyl 2-chloro-2,3,3,3-tetrafluoro-(*III*), 2,3-dichloro-2,3,3-trifluoro-(*IV*), 2,2,3-trichloro-3,3-difluoro-(*V*), 2,3,3,3-tetrafluoro-(*VI*) and 3-chloro-2,3,3-trifluoropropanoate (*VII*) were measured in 0·5M-HCl in aqueous methanol (80% vol; 76% wt) at 40, 50 and 60°C. The relative rate constants, k_{rel} (50°C), (for the propanoate *III*, $k_{H^+} = 4·3 . 10^{-5}$ l . mol^{-1} s^{-1}; $k_{rel} = 100$) are 311, 100, 38, 9·4, 44 and 15 for the esters *II*, *III*, *IV*, *V*, *VI* and *VII*, respectively (experimental error ±9%). It was found that $k_{rel} = \alpha\beta$ where α and β are the following factors for groups in the position 2 and 3: CClF 10, CHF 4·2, CCl_2 2·8, CF_3 10 and $CClF_2$ 3·6. The rate constants obey the isokinetic relationship. For the ester *III* the dependence of $\log k_{obs}$ on logarithm of hydrogen chloride concentration is linear at concentrations 0·08–2·4 mol l^{-1} which, together with high activation entropy $\Delta S^{\neq}$ for the esters *III*–*VII* (−167 to −217 J mol^{-1} K^{-1}), shows that the hydrolysis proceeds by an $A_{AC}2$ mechanism.

Hydrolysis of esters of fluorinated carboxylic acids has been kinetically investigated in neutral[1-9], basic[10-13] and acid[14-16] media. Fluoroacetates have been studied[1-16] most often, their reactivity being compared[4,6,7,10-12,14] with the corresponding chloroacetates. Thus, *e.g.*, neutral hydrolysis of chlorinated acetates is about an order of magnitude[4,7] slower. The rate of neutral hydrolysis of perfluoroacetates decreases with increasing length of the perfluorinated chain[2,8]. Under the same conditions, the rate decreases with increasing length of the unbranched alkyl and this relationship can be linearly correlated[2]. In the acid hydrolysis of fluorinated acetates the effect of the acyl on the reaction rate was not proportional to the number of fluorine atoms[1], the reaction being faster for difluoro- and trifluoroacetate but slower for monofluoroacetate as compared with ethyl acetate. A remarkable effect was observed[15] in acid hydrolysis of phenyl trifluoroacetate. In this case, the dependence of the monomolecular reaction rate on concentration of mineral acid exhibited a marked maximum at about 1 mol l^{-1} and it could not be correlated with the acidity function H_0. With the methyl ester, this effect was even more pronounced[16].

In connection with the mentioned results a study of acid-catalyzed hydrolysis of methyl fluoropropanoates, containing both fluorine and chlorine atoms, was of interest. We investigated therefore a series of the following esters: methyl 2-chloro-2,3,3,3-tetrafluoropropanoate (*III*), methyl 2,3-dichloro-2,3,3-trifluoropropanoate

(*IV*), methyl 2,2,3-trichloro-3,3-difluoropropanoate (*V*), methyl 2,3,3,3-tetrafluoropropanoate (*VI*) and methyl 3-chloro-2,3,3-trifluoropropanoate (*VII*). Methyl propanoate (*II*) was chosen as the reference compound. The hydrolysis was carried out in aqueous methanol in which the esters *III* – *VII* were well soluble (Fig. 1). Since at room temperature the fluorinated propanoates were hydrolyzed up to 30 times more slowly than methyl propanoate, and the experimental error was thus very large, we performed the measurements at 40 – 60°C. In an excess of mineral acid the hydrolysis can be considered as pseudomonomolecular reaction, described by the rate constants k_{obs} (s^{-1}).

EXPERIMENTAL

The temperature was measured with an accuracy of ±0·05°C. Gas-liquid chromatography was carried out on a Chrom 41 chromatograph (Laboratorní přístroje, Prague; FID, stainless steel columns, internal diamater 0·3 cm, carrier gas nitrogen). ^{1}H NMR spectra were taken in deuteriochloroform on a Varian XL-100-15 instrument (Palo Alto), ^{19}F NMR spectra were recorded using CCl_3F as standard. Kinetic measurements were performed in a U-10 ultrathermostat (Mechanik Prüfgeräte, Medingen), accuracy ±0·05°C. Acid-base titrations were carried out on an OP-202/2 pH-meter (Radelkis, Budapest).

Chemicals: Methyl 2-chloro-2,3,3,3-tetrafluoropropanoate (*III*), methyl 2,3-dichloro-2,3,3-trifluoropropanoate (*IV*), methyl 2,3,3-trichloro-3,3-difluoropropanoate (*V*), methyl 2,3,3,3-tetrafluoropropanoate (*VI*) and methyl 3-chloro-2,3,3-trifluoropropanoate (*VII*) were prepared according to the described procedures[17]. Purity of the esters *I* – *VII* was checked by gas-liquid chromatography and NMR spectra; prior to the hydrolysis the esters *III* – *VII* were distilled under diminished pressure. The propanoate *III* contained about 0·5% of *VIII*, the propanoate *IV* was contaminated with about 5% of *VIII* and 1% of $CCl_2F-CF_2-COOCH_3$, the propanoate *VI* contained less than 1% of *III* and the compound *VII* about 2% of $CF_3-CHCl-COOCH_3$.

Measurements of hydrolysis rates. The solubility of the ester *IV* was measured in aqueous methanol, acetone, dioxane and tetrahydrofuran at 20°C. As seen from Fig. 1, the desired 10%

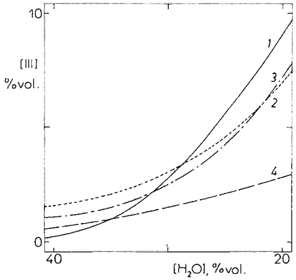

FIG. 1

Solubility of $CClF_2-CClF-COOCH_3$ (*IV*) in aqueous organic solvents: *1* methanol, *2* acetone, *3* dioxane, *4* tetrahydrofuran solubility of the ester is best achieved in aqueous methanol. For kinetic measurements we used an 80 : 20 mixture of methanol and water, corresponding to the weight ratio 76 : 24. Concentration of hydrogen chloride in the reaction mixture was about 0·5 mol l^{-1} and concentration of *I*–*VII* was also approximately 0·5 mol l^{-1}.

A thermostated solution of hydrochloric acid (2·5836 g; 2·027M-HCl) was placed into a 10 ml flask, followed by thermostated methanol (6·4034 g) and finally the halogenopropanoate *IV* (1·0474 g). Because of different density of the components, two layers formed which were mixed at the zero time. From the homogeneous mixture 1 ml samples were withdrawn and titrated with 0·02028M-$Ba(OH)_2$:

t, s	60	780	1 680	2 880	4 080	5 280	5 880	7 740
V, ml	11·75	11·86	11·89	12·05	12·11	12·29	12·31	12·70

The dependence of hydrolysis rate of the ester *III* on acid concentration was measured analogously. The exact concentration of the acidic solutions was determined by acidobasic titration ($Na_2B_4O_7.10\ H_2O$ as standard).

Processing of results. First, the consumption of the hydroxide, V_0, at the time $t = 0$ was calculated by linear regression of ln V *versus* t. Further, for each pair of the values V_i and t_i the concentration of the ester, c_i, was calculated. In calculation of the constants k_{obs} by linear regression it was necessary to exclude points at the end of the measurements because here a reverse reaction or possibly an autocatalytic effect of the acid liberated from the esters *III*–*V* could interfer. For this reason, the differential rate constants k_i for the concentration change Δc during the time Δt were calculated according to the relation

$$k_i = -\frac{\Delta c}{\Delta t}\frac{1}{c} = -\frac{c_i - c_{i-1}}{t_i - t_{i-1}} \cdot \frac{2}{c_i + c_{i-1}} .$$

When at higher t values the plot of k_i against t was not parallel with the time axis, the corresponding values were excluded from the calculation. The rate constants k_{obs} were calculated by linear regression of ln (c_i) upon t and from them the rate constants $k_{H(+)}$ (l mol^{-1} s^{-1}) were calculated (Table I). The same procedure was used for calculation of dependence of hydrolysis rate of the ester *III* on the concentration of the acid.

RESULTS AND DISCUSSION

The order of the rate constants $k_{H(+)}$ is the same at 40, 50 and 60°C (Table I). The esters *III*–*VII* react more slowly than methyl propanoate. Both in pentahalogenopropanoates (*III*–*V*) and tetrahalogenopropanoates (*VI* and *VII*), the halogen-containing groups in the α- or β-position relative to the carboxyl affect in the same sense the hydrolysis rate. We tried to express this effect as a ratio of the corresponding rate constants. The results are shown in Table II. If a chosen group in the α- or β-position is assigned a relative value, we get values of the factors for the other groups:

$—CClF— >$	$—CHF— >$	$—CCl_2—$	$CF_3— >$	$CClF_2—$
$\alpha = 10$	4·2	2·8	$\beta = 10$	3·6

The relative rate constant of a compound of the type $C_{(\beta)}$—$C_{(\alpha)}$—$COOCH_3$ is then a product of both these factors, *i.e.* $k_{rel} = \alpha\beta$. The thus-obtained k_{rel} values (Table I) for the studied series agree well with the experimental values their deviations being smaller than the experimental error. Using these factors we calculated the rate constant $k_{H(+)}$ for methyl 2,2-dichloro-3,3,3-trifluoropropanoate (*VIII*; Table I). The factors α and β comprise all effects (inductive, electrostatic and steric[18]) of the halogenated group on the ester group reactivity.

The experimental rate constants were determined with a relatively large experimental error. For this reason – and also because they were determined at only three temperatures – we do not calculate the activation parameters for the single compounds. In general, the activation enthalpy ΔH^{+} of the esters *I*–*VII* ranges from

TABLE I

Rate constants, k_{H^+}, for acid hydrolysis of esters *I*–*VIII* (concentration of HCl 0·48–0·51mol. .l^{-1})

	Ester	$k_{H^+} = k_{obs}/[HCl] \, . \, 10^5 \pm 9\%^a$			k_{rel} 50°C	k_{rel} calc.
		40°C	50°C	60°C		
I	$CH_3COOC_2H_5$	12	24	36	364	—
II	$CH_3CH_2COOCH_3$	13	20·5	32	311	—
III	CF_3—CClF—$COOCH_3$	4·3	6·6	10·6	100	100
IV	$CClF_2$—CClF—$COOCH_3$	1·5	2·5	4·4	38	36
V	$CClF_2$—CCl_2—$COOCH_3$	0·45	0·7	1·3	9·4	10
VI	CF_3—CHF—$COOCH_3$	1·6	2·9	5·3	44	42
VII	$CClF_2$—CHF—$COOCH_3$	0·78	0·98	1·3	15	
VIII	CF_3—CCl_2—$COOCH_3$	—	1·85[b]	—	—	28

[a] Mean of two measurements; [b] calculated using k_{rel}.

TABLE II

Effect of groups on the rate of acid hydrolysis of halogenopropanoates *III*–*VII* (50°C, concentration of HCl 0·5 mol l^{-1})

Parameter	$CF_3/CClF_2$	$CClF/CCl_2$	$CClF/CHF$
Ratio of	*III*/*IV* 2·65	*IV*/*V* 3·53	*III*/*VI* 2·28
rate constants	*VI*/*VII* 2·91	— —	*IV*/*VII* 2·5
Mean	2·78	3·53	2·39

37·6 to 56·2 kJ mol^{-1} and the activation entropy $\Delta S^{\neq}$ is in the region -167 to -217 J mol^{-1} K^{-1}, the corresponding parameters for ethyl acetate (*I*) and methyl propionate (*II*) lying inside the mentioned intervals.

To verify that the esters *II* – *VII* are hydrolyzed by the same mechanism, we used the isokinetic relation[19] for the mutual dependence of rate constants at two temperatures ($\ln k_{H(+)}$ at T_2 vs $\ln k_{H(+)}$ at T_1). For all combinations of temperatures (40, 50 and 60°C) the slope of this linearized relationship is in the critical region[19] where its small change (due *e.g.* to experimental errors) affects enormously the magnitude of the calculated isokinetic temperature T_β. From the correlation of rate constants at 40 and 60°C we calculated the isokinetic temperature $T_\beta = 97$ K (slope $b = 1·027$, correlation coefficient $r = 0·986$). For 40 and 50°C the following parameters were found: $T_\beta = 200$ K, $b = 1·055$, $r = 0·996$, for 50 and 60°C: $T_\beta = -751$ K, $b = 0·979$, $r = 0·996$ (here the isokinetic temperature is negative which is not exceptional[19,20]). The result of the correlation shows[19,20] that the observed values do not contradict a common mechanism.

Since the hydrolysis rates for phenyl trifluoroacetate[15] and methyl trifluoroacetate[16] depend anomalously on the concentration of the mineral acid, we checked whether an analogous anomaly can be found for the tetrafluoropropanoate *III*. As shown in Fig. 2, in the region 0·08 – 1·1 mol l^{-1} the rate constant of the pseudomonomolecular reaction, k_{obs}, depends linearly on hydrogen chloride concentration and only then the dependence deviates from the linear course. At 2·4 mol l^{-1} the curve obviously still does not reach its maximum.

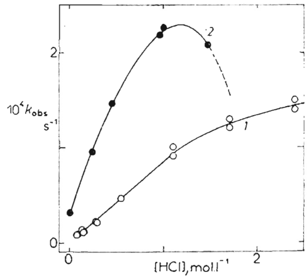

FIG. 2

Dependence of rate constant of acid hydrolysis, k_{obs}, on hydrogen chloride concentration: *1* CF_3–CClF–$COOCH_3$ (*III*), 2 CF_3–$COOCH_3$ (see ref.[16])

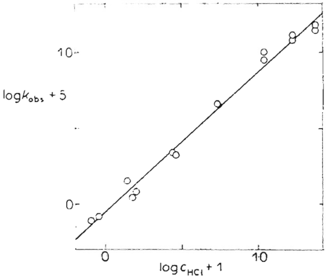

FIG. 3

Plot of rate constant, k_{obs}, for ester *III* against hydrogen chloride concentration

For a decision between the hydrolytic mechanisms A1 and A2, one of the criteria is the linear dependence of log k_{obs} on the acidity function[21] H_0 according to the Zucker–Hammett hypothesis[22,23] or an analogous dependence on the logarithm of the mineral acid concentration (log c_{HCl}). In the region of hydrogen chloride concentrations up to 1 mol l^{-1}, the plot of the acidity function H_0 against log c_{HCl} is linear both for water[21] and for aqueous methanol[24] as solvents. We checked graphically that the acidity function for hydrochloric acid changes in the range 25–50°C only negligibly as compared with the experimental error of our measurements. Further, our considerations were based on the fact that acidity functions in an aqueous solution correlate linearly[25] with those for aqueous solvents and that H_0 changes with the methanol or ethanol content also linearly[26]. Since we found no published values of H_0 for aqueous methanol of the concentration employed by us, we approximated them by the values for a solution of hydrogen chloride in 50% aqueous ethanol[27,28]. The obtained dependence of log k_{obs} on acidity function is linear up to hydrogen chloride concentration of 1·5 mol l^{-1} and then it deviates markedly from the linearity. On the other hand, the log k_{obs} values correlate well with the log c_{HCl} values (Fig. 3; $r = 0{\cdot}9969$). This fact supports the assumed A2 mechanism for hydrolysis of the esters *II–VII*. In the light of the previous results[15,16,23,29,30] it is evident that the reaction involves an acyl-alkoxyl bond fission, *i.e.* an $A_{AC}2$ mechanism[23,31] in which the rate-determining step is reaction of the protonated ester with water (Scheme 1).

$$R_{ClF}\text{—COOCH}_3 + H_3O^+ \xrightleftharpoons{\text{fast}} [R_{ClF}\text{—C(OH)OCH}_3]^{(+)} + H_2O$$

$$[R_{ClF}\text{—C(OH)OCH}_3]^{(+)} + 2\,H_2O \xrightleftharpoons{\text{slow}} R_{ClF}\text{—C(OH)}_2\text{OCH}_3 + H_3O^+$$

R_{ClF} = polychlorofluoroalkyl

SCHEME 1

Another criterion for assignment of the bimolecular mechanism $A_{Ac}2$ is the large activation entropy $\Delta S^{\ddagger}$ which usually[23,32] amounts to −80 to −150 J mol^{-1} K^{-1} (whereas for a monomolecular mechanism it does not exceed −60 J mol^{-1} K^{-1}). In our case these values are even higher (−167 to −217 J mol^{-1} K^{-1}), corresponding numerically to those for neutral hydrolysis of methyl esters of perfluoroacids[3] in 70% aqueous acetone or hydrolysis of alkyl trifluoroacetates[4,6,8] in aqueous dimethyl sulfoxide, containing more than 50% (vol) of dimethyl sulfoxide. Since also for ethyl acetate and methyl propanoate we observed unusually high $\Delta S^{\ddagger}$ values, we conclude that they reflect specific solvation of the activated complex in the given medium.

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