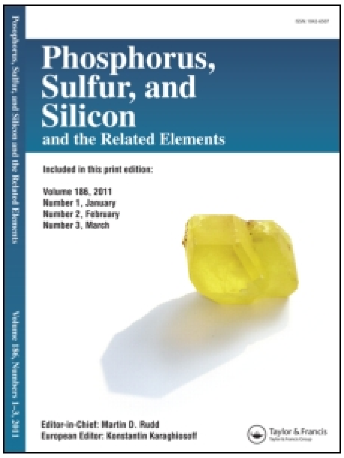

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Kinetics of Spontaneous Hydrolysis of O-(2,2-Dimethylcyclopentyl)-methylfluorophosphonate and of Hydrolysis During Constant pH Value of the Reaction Medium

Boban Ceković[a]; Bratislav Jovanović[b]; Zoran Luković[a]
[a] Military Technical Institute, Belgrade, Yugoslavia [b] Faculty of Technology and Metalurgy, Belgrade, Yugoslavia

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KINETICS OF SPONTANEOUS HYDROLYSIS OF O-(2,2-DIMETHYLCYCLOPENTYL)-METHYLFLUOROPHOSPHONATE AND OF HYDROLYSIS DURING CONSTANT pH VALUE OF THE REACTION MEDIUM

Boban Ceković,[a] *Bratislav Jovanović,*[b] *and Zoran Luković*[a]
Military Technical Institute, Belgrade, Yugoslavia[a] *and Faculty of Technology and Metalurgy, Belgrade, Yugoslavia*[b]

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Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in dilute aqueous solution was investigated. Rates of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate were measured as a function of pH (in the range from 3 to 9 and without keeping the pH-value constant—in a spontaneous hydrolysis) and temperature (in the range from 25°C to 40°C). Objective of these investigations was to simulate real processes of degradation of highly toxic compounds in nature, getting information about rates of degradation, in order to obtain most efficient systems for their removal.

Keywords: Hydrolysis; kinetics; O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate; organic phosphorus compounds

One of the less known organic compounds containing phosphorus is O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, a possible member of a recently investigated group of "intermediate volatile agents" (IVA).[1–3]

The reaction of hydrolysis giving non-toxic products is especially significant in studying of degradation of highly toxic compounds of penta valent phosphorus—esters of methylfluorophosphonic acid.

The rate of hydrolysis of methylfluorophosphonic acid esters is important for determining their persistence in the environment, which in turn, is relevant for understanding the threat posed by their use.[4]

Address correspondence to B. Jovanović, Faculty of Technology and Metalurgy, Karnegijeva 4, P.O. Box 494, Belgrade, Yugoslavia.

Literature[5–9] reveals that the hydrolysis of known analogues of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate is irreversible and depends on the pH-value of the reaction medium.

Because the hydrolysis of analogues of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate is catalyzed by several ions, instead of investigating the reaction in various buffer solutions, the hydrolysis has been monitored by an electrometric pH-stat method. Kinetics of spontaneous hydrolysis was followed by measuring the change of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate concentration according to the degree of inhibition of buthyrylcholinesterase, using UV/Vis spectrophotometry.

RESULTS AND DISCUSSION

Determining the Rate of Hydrolysis of O-(2,2-Dimethylcyclopentyl)-methylfluorophosphonate at Constant pH-Value of Reaction Medium

Rates of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate were investigated at constant pH-value of reaction medium and at temperatures 25°C, 35°C, and 40°C.

For determination of pseudo-first-order rate constant k'_1 (min^{-1}) for hydrolysis in a large excess of water (at C^+_H = const. or C^-_{OH} = const.), the equation for first-order reactions was applied[10,11]

$$\ln[C_0/C] = k'_1 t \tag{1}$$

where:

C_0 = initial concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, mol/dm^3,
C = concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in time, mol/dm^3,
t = duration time of the reaction, min.

Whereby during hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate molecule-hydrogen fluoride and O-(2,2-dimethylcyclopentyl)-methylphosphonic acid are released (according to compounds reported for its analogues), it is assumed that consumption of sodium-hydroxide, for neutralization of the two acids, is equal to the twofold amount of disrupted molecules of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate. On the basis of volume of titrant spent in time, a change in concentration of O-(2,2-dimethylcyclopentyl)-

methylfluorophosphonate is calculated using equation:

$$C = \frac{n - \frac{V_T \cdot C_T}{2}}{V_{DV} + V_{PD} + V_T} \tag{2}$$

where are:

n = initial amount of moles of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in total volume of reaction mixture, mol,
V_T = consumed (spent) volume of titrant (NaOH solution) in time, dm^3,
C_T = concentration of sodium hydroxide in solution being used as titrant, mol/dm^3,
V_{DV} = volume of distilled water, dm^3,
V_{PD} = volume of previously added solution of NaOH (or HCl for acidic conditions) for adjusting of initial pH-value, dm^3.

By substitution of Eq. 2 in Eq. 1, expression 3 is obtained and applied in concrete cases:

$$\ln\left(\frac{C_0(V_{DV} + V_{PD} + V_T)}{n - \frac{V_T \cdot C_T}{2}}\right) = k_1' \cdot t \tag{3}$$

Satisfactory agreement of experimental data and Eq. 3 confirms the pseudo-first order of the reaction (first order for the reaction of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate), where the slope represents the pseudo-first-order rate constant k_1', which can be seen in Figure 1.

On the basis of experimentally monitored consumption of the titrant volume, values for k_1' (min^{-1}) were calculated and presented in Table I.

According to reference,[8] the change of ionic strength during reaction ($\mu < 5 \cdot 10^{-3}$, with activity coefficient of ions in the reaction mixture—$f > 0{,}935$, calculated using Hückel equation[12] for case $\mu < 0,01$, where $\log f = -0,5\, z^2 \mu^{1/2}$, and z represents electron charge of an ion), does not have significant influence on the reaction rate (± 5 %), and therefore can be disregarded.

Based upon kinetic data, activation parameters were calculated: energy of activation E_a, frequency factor A, entropy of activation $\Delta S^{\#}_{25}$, Gibbs's free-energy of activation $\Delta G^{\#}_{25}$ and enthalpy of activation $\Delta H^{\#}_{25}$.[10,11]

The energy of activation and the frequency factor were calculated using the slope of a line defined by the Arrenius equation (ln k_1' versus the reciprocal value of the absolute temperature in degrees K):

$$\ln k_1' = (E_a/R) \cdot 1/T + \ln A \tag{4}$$

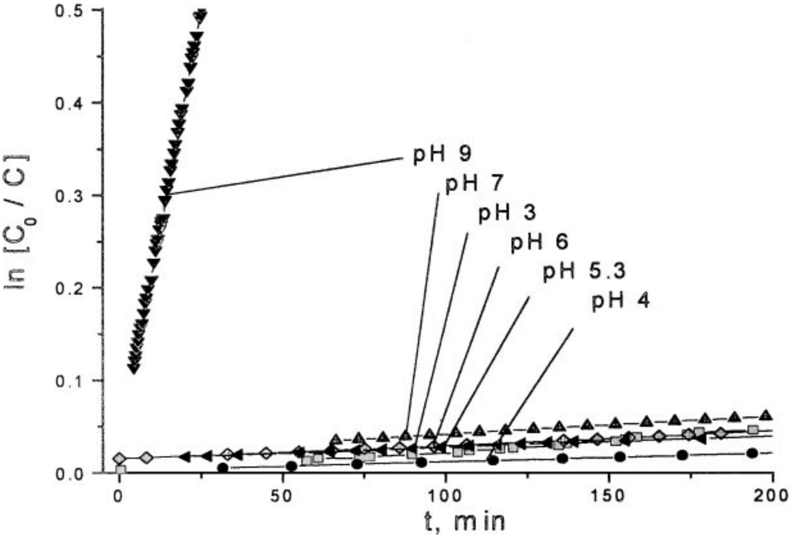


FIGURE 1 Kinetics of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate under different constant pH-values on 25°C, observed as pseudo-first-order reaction.

where:

R = common gas constant

For calculation of the entropy of activation the following equation was used:

$$\Delta S^{\#}_{25} = (\ln[k'_1 h/KT] + E_a/RT)\, R \tag{5}$$

TABLE I Rate Constants for Hydrolysis of O-(2,2-Dimethylcyclopentyl)-methylfluorophosphonate under Constant pH-Values of the Reaction Medium

PH-value of the reaction medium	$k'_1 10^4$ (min^{-1})		
	25°C	35°C	40°C
3.0	2.04	5.15	7.16
4.0	0.89	2.28	4.28
5.3	0.71	2.35	4.85
6.0	1.22	2.75	4.98
7.0	2.07	5.55	8.56
9.0	12.6	280.0	5.50

TABLE II Activation Parameters for the Hydrolysis of O-(2,2-Dimethylcyclopentyl)-methyl-fluorophosphonate at Constant pH Values of the Reaction Medium

pH	E_a [kJ/mol]	A	$\Delta H^{\#}_{25}$ [kJ/mol]	$\Delta G^{\#}_{25}$ [kJ/mol]	$\Delta S^{\#}_{25}$ [J/molK]
3.0	65.9 ± 4.25	$1.225 \cdot 10^6$	63.4	107.7	−148.75
4.0	79.9 ± 7.3	$142.9 \cdot 10^6$	77.4	105.9	−95.70
5.3	97.9 ± 6.2	$169.4 \cdot 10^9$	95.4	107.3	−40.10
6.0	74.4 ± 8.5	$20.6 \cdot 10^6$	71.9	105.7	−113.45
7.0	73.8 ± 1.3	$29.7 \cdot 10^6$	71.3	103.8	−109.15
9.0	73.9 ± 11.5	$177.0 \cdot 10^6$	71.4	93.6	−74.50

where:

h = Planck constant, K = Boltzman constant.

The enthalpy of activation and the Gibbs's free-energy of activation were calculated by following equations:

$$\Delta H^{\#}_{25} = E_a - RT \tag{6}$$

$$\Delta G^{\#}_{25} = \Delta H^{\#}_{25} - \Delta S^{\#}_{25} T \tag{7}$$

The entropy of activation was calculated by using pseudo-first-order rate constants on 25°C.

The values of activation parameters are presented in Table II. Rate constants dependence from pH values are presented in Figure 2.

On the basis of kinetic data and calculated activation parameters, nucleophilic substitution reaction of the $S_N2(P)$-type was established, proceeding through three different mechanisms depending on the pH-value of the reaction medium.

In alkaline conditions (pH $>$ 6.5) the nucleophilic attack of the negative hydroxide ion at the electron deficient phosphorus atom is dominant, where the reaction rate increases with rising of pH-value, i.e., with higher concentration of the negative hydroxide ion.[6,8,13–15]

In neutral conditions (4.5 $<$ pH $<$ 6.5) the nucleophilic attack of the polar water molecule is dominant, with a negligible change of reaction rate in that range.[6,13–17]

In acid conditions (pH $<$ 4.5) a two-step, catalytic mechanism prevails, where protonated oxygen atom facilitates the nucleophilic attack on phosphorus atom. In this case, the rate of the reaction depends on the degree of protonation of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, which is in accordance with literature references for analogous compounds.[6,18] With further drop of the pH-value,

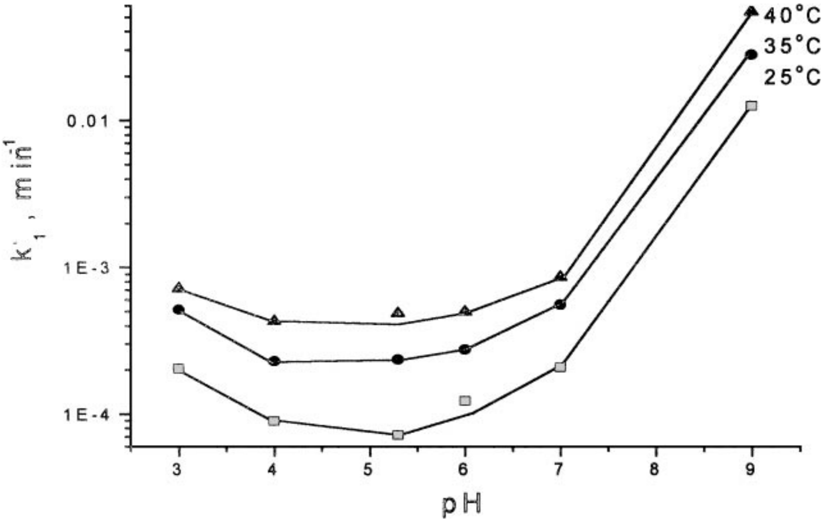


FIGURE 2 Dependence of pseudo-first-order rate constants of hydrolysis of O-(2,2-dimethyl-cyclopentyl)-methylfluorophosphonate on the pH-values at different temperatures.

and rise in the concentration of hydrogen positive ion, the rate of reaction increases.[6,17,18]

According to the assumption that all three mechanisms participate in hydrolysis reactions, depending on the pH-value of the reaction medium, experimentally determined overall pseudo-first-order rate constants k'_1(min^{-1}) on different temperatures can be described by Eq. 8:[8,17,19]

$$k'_1 = k_a C_H + k'_{H_2O} + k_b C_{HO} \tag{8}$$

where:

k_a = hydrolysis rate constant in acid conditions, dm^3/mol min
k'_{H_2O} = hydrolysis rate constant in neutral conditions, 1/min
k_b = hydrolysis rate constant in alkaline conditions, dm^3/mol min
C_H = hydrogen ion concentration, mol/dm^3
C_{HO} = hydroxide ion concentration, mol/dm^3

Considering dilution and the fact that during the whole reaction, the activity coefficients have values from 0.935 to 0.992 ($\mu < 0.005$), it can be approximated that hydrogen ion activity $a_H \approx C_H$.

Since pH $= -\log a_H$, and $k_w = a_H\, a_{HO}$ (a_{HO} – hydroxide ion activity, k_w – ionic product of water, i.e. p$k_w = -\log k_w$), in order to determine k_a,

TABLE IIIa Partial Rate Constants of Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophospho-nate under Constant pH-Values of Reaction Medium (for Range of pH-Values from 3.0 to 9.0) if Change of Ionic Product of Water is Disregarded

Temperature °C	Partial rate constants		
	k_a (dm^3/mol min)	k'_{H_2O}(1/min)	k_b (dm^3/mol min)
25	0.119	$0.84 \cdot 10^{-4}$	$1.25 \cdot 10^3$
35	0.272	$2.39 \cdot 10^{-4}$	$2.78 \cdot 10^3$
40	0.309	$4.06 \cdot 10^{-4}$	$4.58 \cdot 10^3$

k'_{H_2O} and k_b, Eq. 8 can be written in the following form:

$$k'_1 = k_a 10^{-pH} + k'_{H_2O} + k_b 10^{-(pk_w - pH)} \tag{9}$$

Using the least-square method approximation (linear curve fitting) partial second-order rate constants were determined and presented in Table IIIa (applying $k_w = 10^{-14}$ for all three temperatures).

It is obvious that the hydrolysis rate constants in alkaline conditions are the highest, hydrolysis rate constants in acid conditions are in-between, and the hydrolysis rate constants in neutral conditions are the lowest, which is in agreement with the overall rate of hydrolysis in a range of pH-values, i.e., participation of mentioned mechanisms in the overall hydrolysis at specified pH-values are expected.[13,17]

But, when using the correct values of ionic product of water at different temperatures (for 25°C $k_w = 10^{-14}$, 35°C $k_w = 2.083 \cdot 10^{-14}$, and for 40°C $k_w = 2.95 \cdot 10^{-14}$), it is determined that the values of the rate constants in alkaline conditions at 35°C ($k_b = 1.40 \cdot 10^3$ dm^3/mol min), and at 40°C ($k_b = 1.86 \cdot 10^3$ dm^3/mol min) are different from the values presented in Table IIIa. The values of hydrolysis rate constant in acid and neutral conditions do not change with the use of the correct values of the ionic product of water, because of their independence on temperature influenced change of ionic product of water at constant pH-value (a_H = const., but $a_{HO} \neq$ const.). Lower values of hydrolysis rate constant in alkaline conditions at 35°C and 40°C, compared to those in Table IIIa are the consequence of the fitting of data at different temperatures and at different ionic products of water (different values of C_{HO}), and although these are the most accurate constants for each pH-value on specific temperature, it is not possible to calculate accurately the activation parameters for the rate of alkaline hydrolysis (because $C_{HO} \neq$const., i.e., the pOH-value has changed). For determination of activation parameters for alkaline hydrolysis, correlation of

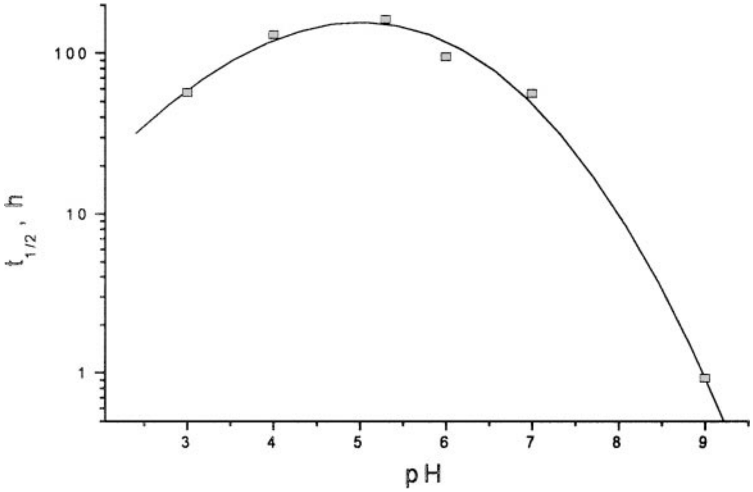


FIGURE 3 Dependence of half-lives of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluoro-phosphonate on pH-values of reaction mixture on 25°C.

pseudo-first-order rate constants with pOH-values is established (and not with pH values as in Figure 3), and on the basis of interpolation on pOH 5 (pH 9 on 25°C), pseudo-first-order rate constants on 35°C ($k_1' = 0.0145\ \text{min}^{-1}$) and 40°C ($k_1' = 0.0188\ \text{min}^{-1}$) were determined. Using these values, and taking in consideration the known values for k_a and k'_{H_2O}, using the equation:

$$k_b = \frac{k_1' - \left(k_a 10^{-(pk_w - pOH)} + k'_{H_2O}\right)}{10^{-pOH}} \tag{10}$$

values of k_b were obtained for constant pOH-values presented in Table IIIb.

On the basis of values from Table IIIb, by using Eqs. 4 to 7, activation parameters were calculated for each of partial rate constant and are presented in Table IV.

TABLE IIIb Partial Rate Constants for the Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate at Constant pH and pOH-Values of Reaction Medium

	Partial rate constants		
Temperature °C	k_a (dm^3/mol min)	k'_{H_2O}(1/min)	k_b (dm^3/mol min)
25	0.119	$0.84 \cdot 10^{-4}$	$1.25 \cdot 10^3$
35	0.272	$2.39 \cdot 10^{-4}$	$1.43 \cdot 10^3$
40	0.309	$4.06 \cdot 10^{-4}$	$1.84 \cdot 10^3$

TABLE IV Activation Parameters for the Partial Rate Constants for Hydrolysis of O-(2,2-dimethyl-cyclopentyl)-methylfluorophosphonate under Constant pH-Values of Reaction Medium

Reaction rate constants	E_a [kJ/mol]	$\ln A$	$\Delta H^{\#}_{25}$ [kJ/mol]	$\Delta G^{\#}_{25}$ [kJ/mol]	$\Delta S^{\#}_{25}$ [J/molK]
k_a	50.1 ± 9.7	14.06	47.6	87.6	−134.2
k'_{H_2O}	81.0 ± 1.4	15.18	78.5	115	−123.5
k_b	18.9 ± 6.0	10.58	16.3	62.2	−154.1

It is seen from Table IV that values of the change of entropy of activation for acid catalyzed hydrolysis reaction are negative (the activated complex shows significantly a higher degree of order), and the energy of activation is relatively low, which is characteristic for catalyzed reactions and reactions of neutral reagents,[7,20] thus confirming presupposed mechanism being typical for similar compounds.

Significantly higher values of activation energy and negative values of entropy of activation calculated for reaction of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in neutral conditions, can be explained as a reaction of neutral reagents, and higher amount of energy is necessary for achieving of nucleophilic attack of voluminous molecule of water on phosphorus atom from side opposite to P—F bond, which is also complicated because of steric hindrance of 2,2-dimethylcyclopentoxy group bonded to phosphorus atom. Thereby as the degree of freedom of activated complex is less, i.e., transition state is in more orderly, so that the entropy of activation is significantly negative.

The low value of entropy of activation for alkaline hydrolysis (but approximately inside the limits given in literature references for bimolecular reactions[20,21]) appears as a consequence of significantly more arranged state of activated complex and solvent effects. Very low value of activation energy (along with negative entropy of activation) indicates the classical bimolecular reaction of nucleophilic substitution of S_N2 (P) type.

The half-lives of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate depending on pH-values (calculated by $t_{1/2} = \ln 2/k'_1$ and presented in Table V and on Figure 3) indicate that, from the point of decontamination, only alkaline water solutions are applicable, whereby it is necessary to maintain the pH value above 10 (for pH 9 on 25°C $t_{1/2} = 55$ min). Low activation energy indicates a small temperature dependence of reaction rate, so it is possible to use the reaction in a broad temperature range.

TABLE V Halftimes of Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate ($t_{1/2}$) Depending on pH-Values on Different Temperatures (pH-Stat Method)

	$t_{1/2}$, h		
pH	25°C	35°C	40°C
3.0	56.63	22.43	16.13
4.0	129.8	50.67	26.99
5.3	161.8	49.16	23.82
6.0	94.69	42.16	23.20
7.0	55.81	20.82	13.50
9.0	0.920	0.413	0.210

DETERMINATION OF THE RATE OF HYDROLYSIS OF O-(2,2-DIMETHYLCYCLOPENTYL)-METHYLFLUOROPHOSPHONATE IN DISTILLED WATER WITHOUT CONSTANT PH-VALUE OF THE REACTION MEDIUM (SPONTANEOUS HYDROLYSIS)

Since the investigation on the rates of spontaneous hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate was conducted in a large excess of water, the reaction was treated as a pseudo-first-order reaction.[10,11]

Concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate was determined by using of enzyme method, since O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate appeared to be a strong cholinesterase inhibition agent.[1,5] Calibrating chart, presented on Figure 4, was obtained by determination of cholinesterase activity of previously prepared solutions of O-(2,2-dimethyl-cyclopentyl)-methylfluorophosphonate with known concentrations.

By using the measured activities of cholinesterase in Eq. 11, determined from calibrating chart, the concentrations of O-(2,2-dimethyl-cyclopentyl)-methylfluorophosphonate (C in mol/dm^3 units) were obtained. Due to that, and to the low rate of hydrolysis for the range of pH-values between 4,0 and 6,0 , it was possible to use the same method for following of spontaneous hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, as can be seen on Figure 4.

$$C = f_r \cdot \left[0{,}5 - 2{,}701 \cdot \ln\left(\frac{A + 22{,}134}{260{,}65}\right)\right] \tag{11}$$

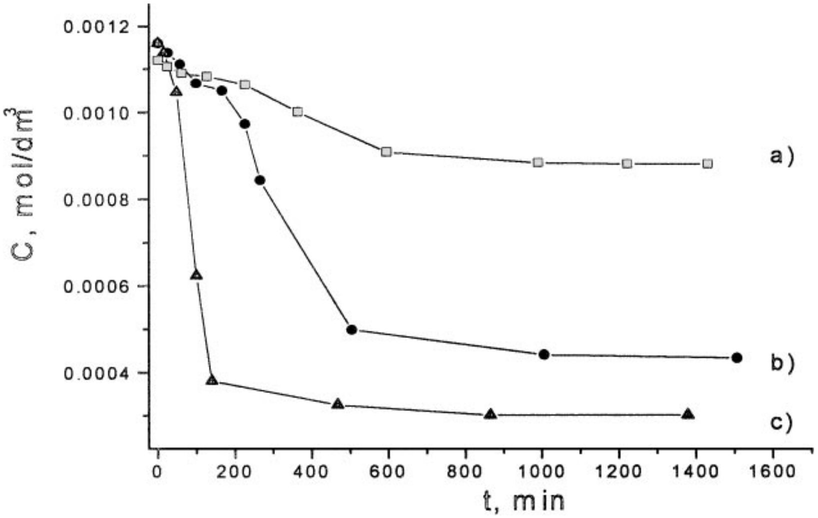


FIGURE 4 Change of concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate (detreminated using degree of cholinesterase inhibition) at spontaneous hydrolysis on 25°C, b) 35°C and c) 40°C.

where:

A = activity of buthyrylcholinesterase (BuChE) after interaction with O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate (mIU/cm^3),
f_r = dilution factor, which equals 0,0003732.

It can be noticed that the change of concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate is analogous to reactions in which auto catalysis by some reaction product appears. Assumption of the auto catalysis reaction can be even better observed by the interpolated chart of concentration change of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate (by using function $y = a/(1 + b \cdot e^{cx})$) given in Figure 5.

In this case, the most probable hydrolysis products are O-(2,2-dimethylcyclopentyl)-methylphosphonic acid and hydrogen fluoride, which are, due to dilution, completely dissociated giving positive hydrogen ions which catalyses hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate.

For an approximated description of the spontaneous hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in water, method for determination of k'_{obs} (min^{-1}) can be used,[10,22] which is determined via the half-lives ($t_{1/2}$, min) of O-(2,2-dimethylcyclopentyl)-

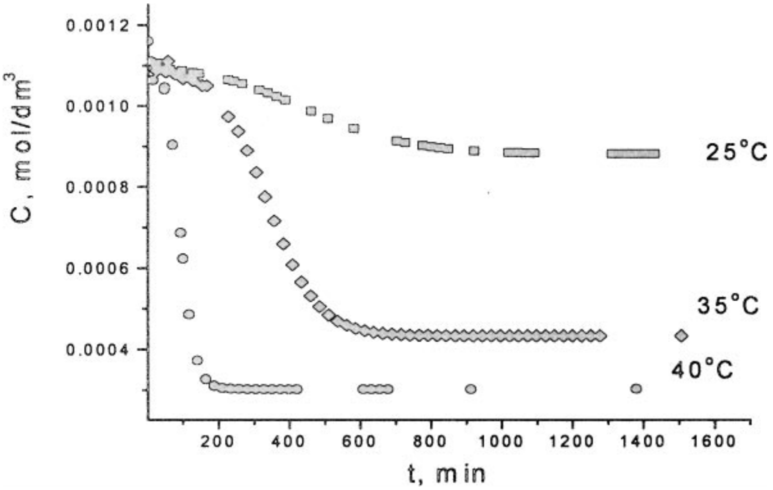


FIGURE 5 Change of concentration (interpolated) of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate during spontaneous hydrolysis.

methylfluorophosphonate and, in case of first-order reaction toward O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, by using the next equation:

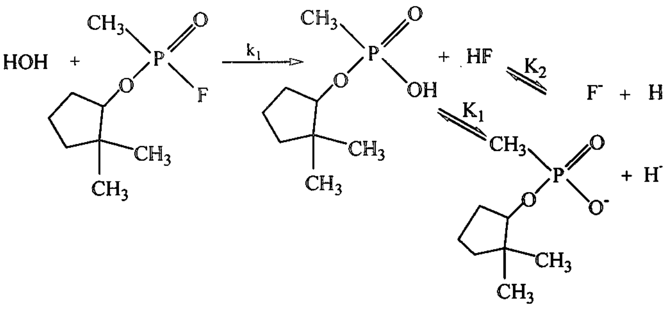
$$k'_{obs} = \ln 2/t_{1/2} \tag{12}$$

In Table VI the half-lives and general rate constant k'_{obs} on different temperatures are presented.

Observing of change of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate concentration in time, values of rate constants k'_{obs}, and also the literature references data for hydrolysis of similar compounds[14,15,22] leads to an assumption of complex and unsteady mechanism of spontaneous hydrolysis that can be described as parallel reaction of hydrolysis by molecules of water (solvent) and acid-catalyzed

TABLE VI Spontaneous Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate-the Half-Lives ($t_{1/2}$) and k'_{obs} Rate Constants

Temperature, °C	$t_{1/2}$, h (min)	k'_{obs} 10^3, min^{-1}
25	67.0 (4020.6)	0.1724
35	12.8 (769.30)	0.9010
40	2.70 (159.30)	4.3500



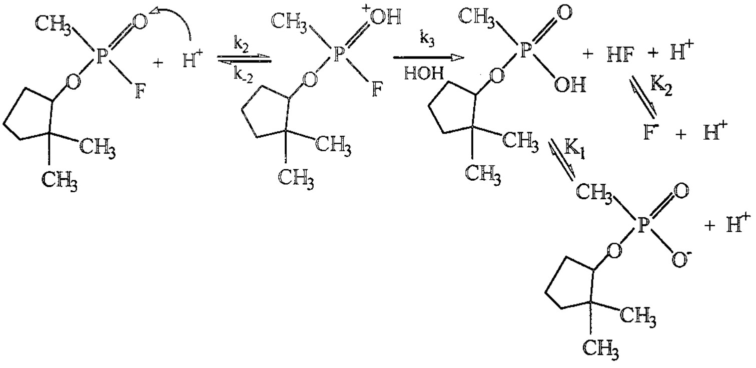
SCHEME 1 Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate by molecules of water—reaction **(1)**.

hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate. In the first part of the reaction (based on a chart in Figure 5), most likely a hydrolysis by polar molecules of water - reaction **(1)** is dominant (Scheme 1), but with participation of reaction **(2)** (Scheme 2). After releasing significant amounts of positive hydrogen ions, reaction **(2)** becomes dominant, but also with participation of reaction **(1)**.

For the assumed mechanism suitable mathematical models for a common autocatalysis reaction[10] represented by equations which follow should be appropriate.

Reaction rate of spontaneous hydrolysis according to the suggested mechanism can be represented by the next differential equations:

$$\frac{-dC}{dt} = k_1C + k_2Ca_H - k_{-2}C_p \tag{13a}$$



SCHEME 2 Acid-catalyzed hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate—reaction **(2)**.

considering the amount of dilution it can be approximated that $C_H \approx a_H$, i.e., initial concentration $C_{Ho} \approx a_{Ho}$, it is

$$\frac{-dC}{dt} = k_1C + k_2CC_H - k_{-2}C_p \tag{13b}$$

where:

C = concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in time, mol/dm^3,
C_p = concentration of protonised O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, mol/dm^3
k_1 = pseudo-first-order rate constant for hydrolysis by water molecules, min^{-1}
k_2 = rate constant for protonization of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, dm^3/mol min
k_{-2} = rate constant for deprotonization of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, dm^3/mol min
k_3 = pseudo-first -order rate constant for hydrolysis of protonised O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, min^{-1}

In Eq. 13b several approximations can be introduced. First one is that constant k_3 has no influence on reaction rate because of almost instant transfer of unstable intermediate compound into products. Along with that constant k_{-2} also loses its significance, i.e., becomes negligible small. On that basis the third component of Eq. 13b is eliminated and Eq. 14 is obtained:

$$\frac{-dC}{dt} = k_1C + k_2CC_H \tag{14}$$

According to the assumption that, because of dilution, acids released as reaction products are completely dissociated, the next equation is being used:

$$C_H = C_{H_0} + 2(C_0 - C) \tag{15}$$

By solving Eq. 14 against C, also using Eq. 15, solutions for rate constants k_1 and k_2 are obtained giving good correlation with experimental data, but it is observed that rate constants are about equal. That indicates that Eq. 14 can be simplified even more to a well-known Eq. 16 for autocatalytic reactions,[11] which, solved by using Eq. 15 gives Eq. 17 obtaining satisfactory correlation to experimental data. In Table VII values for autocatalytic rate constants k_1 are given on

TABLE VII Spontaneous Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate Rate Constants k_1 and Corresponding Activation Parameters

Temperature (°C)	k_1 (dm^3/mol min)	E_a [kJ/mol]	A	$\Delta H^{\#}_{25}$ [kJ/mol]	$\Delta G^{\#}_{25}$ [kJ/mol]	$\Delta S^{\#}_{25}$ [J/mol K]
25	2.80					
35	5.83	79.63 ± 15	$3.74 \cdot 10^{12}$	77.2	80.7	−12
40	14.30					

different temperatures and corresponding activation parameters.

$$\frac{-dC}{dt} = k_1 C C_H \tag{16}$$

$$C = \frac{\frac{1}{2}(C_{H_0} + 2C_0)}{1 + \frac{C_{H_0}}{2C_0} e^{k_1(C_{H_0}+2C_0)t}} \tag{17}$$

Spontaneous hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate has a value for evaluation of natural decontamination effects i.e., decontamination by water which, according to half-life of hydrolysis from reaction degree ($t_{1/2} = 4020$ min i.e., about 2,8 days at 25°C), cannot be applied for decontamination for diluted solutions, as in case of concentrated solutions can be spoken of catalysis effect of hydrogen ions, that is to say about possibility for use in decontamination.

EXPERIMENTAL

Chemicals

- O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate, synthesized by the method described in literature for similar compounds[5–7,9], purity about 98%,
- 1,4-dioxane, p.a., Riedel-de Haën
- sodium-hydroxide, p.a., Merck
- hydrochloric acid, 36%, p.a., Merck
- buffers pH 7.02 ± 0.01, 4.00 ± 0.01 (on 20°C), Radiometer
- 5,5′-dithiobis-2-nitrobenzoic acid (DTNB), p.a., Merck
- buthyrylcholinesterase (BuChE), of horse serum origin, dry, lyophilized, laboratory produced, activity about 200 IU/mg,
- buthyrylthiocholine iodide (BuSChJ), p.a., Merck
- potassium bihydrogen phosphate anh., p.a., Riedel-de Haën
- 2-propyl alcohol, p.a. "Riedel -de Haën"

Prepared Solutions Used

- phosphate buffer pH 7, conc. 0.05 mol/dm^3 (prepared by mixing 6.804 g of potassium bihydrogen phosphate in 500 ml of distilled water (0.1 mol/dm^3), then titrated with solution of sodium-hydroxide using pH-meter and a stirrer until achieving pH 7 and then adding distilled water up to the volume of 1000 cm^3),
- solutions of sodium-hydroxide in distilled water, conc. $2.5 \cdot 10^{-3}$ mol/dm^3, $5 \cdot 10^{-3}$ mol/dm^3, $7.93 \cdot 10^{-3}$ mol/dm^3 and 10^{-2} mol/dm^3,
- basic solution of BuChE, concentration less than 1 mg/cm^3 in distilled water,
- indicator solution, concentration 0.25 mol/dm^3 (prepared by dissolving 5 mg DTNB in phosphate buffer up to 50 cm^3),
- substrate solution, concentration 10^{-2} mol/dm^3 (prepared by dissolving 77.4 mg BuSChJ in distilled water up to 25 cm^3)
- solution **A** prepared by adding certain volume (ensuring the activity of solution **A** 300 ± 10 mIU/cm^3) of basic solution of BuChE in 10 cm^3 normal vessel and supplementing with phosphate buffer
- solution **B** that represents a mixture of substrate solution and indicator solution in ratio 1:2 (v/v).

Kinetic Measurements for Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate under Constant pH-Value of Reaction Medium

Kinetics of hydrolysis was followed by automatic recording titration system[8] in pH-stat mode-acid products formed in hydrolysis are neutralized by addition of alkali solution (titrant-sodium-hydroxide) in a rate that maintains constant pH value of the reaction mixture. The volume of spent titrant is recorded as a function of time. The instrument was Radiometer RTS822, using Radiometer glass electrodes, type G 202 A, as indicator electrode and a saturated calomel electrode, type K 401, as a reference electrode. Fluctuation of pH was generally less than ±0.02 pH units. Thermostat maintained constant temperature in jacketed reaction vessel with precision of ±0.1°C.

After adjusting initial pH-value of reaction mixture to desirable value, volume of 0.2 cm^3 of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate solution in 1,4-dioxane (in ratio 1:19, v/v) was added in reaction vessel. Starting concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in reaction mixture was $\sim 2.2 \cdot 10^{-3}$mol/dm^3.

Kinetic Measurements for Spontaneous Hydrolysis of O-(2,2-dimethylyclopentyl)-methylfluorophosphonate (Without Vonstant pH-Value of Reaction Medium)

The kinetics of hydrolysis was followed spectrophotometrically by indirect determination of the concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate as cholinesterase inhibition agent, using the calibrating chart, previously prepared, as follows:

Calibrating Chart

UV/VIS measuring system GILFORD Impact400E was prepared for the experiments using software for monitoring the cholinesterase inhibition agent concentration by enzyme method. In 10 ml normal vessel, volume of $22 \cdot 10^{-3}$ ml of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate was transferred, added with 2-propyl alcohol up to 10 ml and mixed, thus obtaining basic solution BS. From BS 0.2 ml of solution was transferred in 100 ml normal vessel and filled with 2-propyl alcohol, thus getting operating solution OS. Operating solution is further diluted in distilled water for obtaining measuring points for calibrating chart (solutions S1 do S8).

Measuring system's autosampler automatically adds BuChE (solution **A**) to solutions S1 to S8. BuChE is, during incubation time, being inhibited by O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate which is directly proportional to the concentration of the inhibitor. Afterward, the mixture of BuSChJ and indicator DTNB (solution **B**) was added and the absorbance was measured (depending on concentration of noninhibited BuChE). The values of cholinesterase (BuChE) activity are automatically calculated by the system's software (using the absorbance values), and then are correlated to concentrations of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in solutions S1 to S8 on calibrating chart (Figure 6). Activity of "the blank" is 300 ± 10 mIU/cm^3. As the activity of the sample (solution S1 to S8) is less than the activity of "the blank" so the bigger is the concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate.

Monitoring of Spontaneous Hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate

UV/VIS measuring system GILFORD Impact400E is prepared to work for preparing a calibrating chart. Volume of 10 cm^3 of distilled water (pH 5.5–6.5) was added in jacketeed reaction vessel equipped with suitable cover and magnetic stirrer. Thermostat maintained constant temperature with precision of ±0.2°C. Volume of 0.1 cm^3 of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate solution in 2-propyl

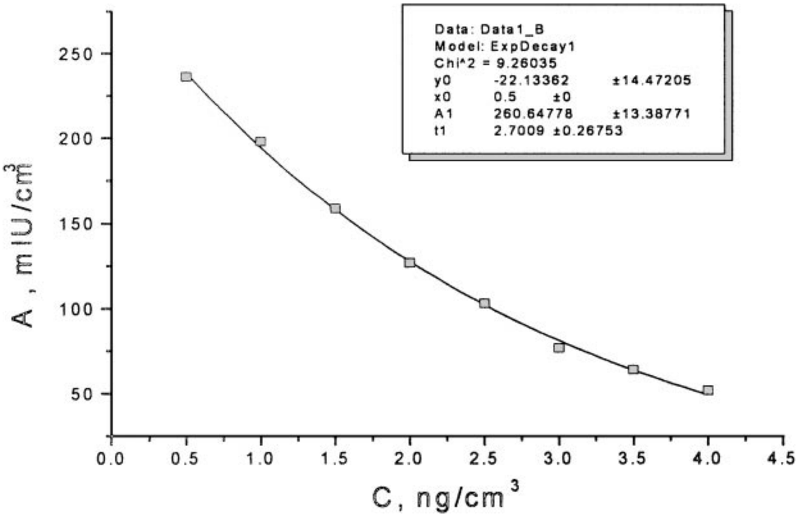


FIGURE 6 Calibrating chart—Correlation of cholinesterase activity and concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate.

alcohol (in ratio 1:49, v/v) was added in reaction vessel. Initial concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in reaction mixture was ~0.9–1.1 · 10^{-3} mol/dm^3.

One minute after adding of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate (and then at every 30–60 min) an amount of 0.2 ml of the reaction mixture is transferred to 10 ml normal vessel and filled up with 2-propyl alcohol. The obtained solution was further diluted with distilled water, thus obtaining measuring sample (initial concentration ~3 ng/ml) to which, in measuring system GILFORD Impact400E, solution **A** (BuChE) was added automatically, and the mixture of BuSChJ and indicator DTNB (solution **B**) was also added and absorbance was measured (depending on concentration of noninhibited BuChE) and activity of cholinesterase was registered. On the basis of cholinesterase activity, concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate was determinated from the calibrating chart.

CONCLUSIONS

1. Rates of hydrolysis of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate under constant pH-value of reaction medium and without maintaining constant pH value were investigated.

2. Pseudo-first-order rate constants were determined, from which hydrolysis rate constant in acid, neutral and alkaline conditions were calculated. Activation parameters were calculated: energy of activation, frequency factor, entropy of activation, Gibbs's free energy of activation, and enthalpy of activation.
3. The rate of hydrolysis increases from neutral conditions toward acid and alkaline conditions, which is in accordance with reference data for similar compounds belonging to a group of alkyl esters of methylfluorophosphonates.
4. Reactions at alkaline conditions have satisfactory reaction rate and the products are less toxic.
5. For the spontaneous hydrolysis without the pH regulations, rate constants were determined from the half-lives of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate (approximattion), as well as from the autocatalytic rate constants. From these, and also from the change of concentration of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate in time parallel reaction mechanism of hydrolysis and auto hydrolysis are postulates. For this complex reaction, activation parameters were also calculated: energy of activation, frequency factor, entropy of activation, Gibbs's free energy of activation, and enthalpy of activation.
6. Reaction of spontaneous hydrolysis is significant for acquirement of knowledge of natural decon-tamination of O-(2,2-dimethylcyclopentyl)-methylfluorophosphonate on surfaces.

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