Kinetics of hydrolysis
of 2-substituted 4,5-dichloro-3-oxo-2H-pyridazines

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The kinetics of hydrolysis of 2-R-4,5-dichloro-3-oxo-2H-pyridazines ($R = CH_3$, C_3H_7, $(CH_3)_2CH$, C_4H_9, $(CH_3)_3C$, C_5H_{11}, C_6H_{11} (cyclo), C_6H_5, CH_2—C_6H_5, CH_2—C_6H_4—4-CH_3) has been studied. The products of the reaction were found to be the respective 2-R-4-chloro-5-hydroxy-3-oxo-2H--pyridazines, *i.e.* only the chlorine bound in position 5 entered the reaction. The probable mechanism and the effect of the substituent on hydrolysis have been explained.

Изучена кинетика гидролиза 2-R-4,5-дихлор-3-оксо-2H-пиридази-нов ($R = CH_3$, C_3H_7, $(CH_3)_2CH$, C_4H_9, $(CH_3)_3C$, C_5H_{11}, C_6H_{11} (цикло), C_6H_5, CH_2—C_6H_5, CH_2—C_6H_4—4-CH_3). Обнаружено, что продуктами реакции являются соответствующие 2-R-4-хлор-5-гидрокси-3-оксо--2H-пиридазины, т. е. в реакцию вступал только хлор, находящийся в положении 5. Объясняется вероятный механизм и влияние замес-тителя на гидролиз.

It is known that 2-substituted 4,5-dichloro-3-oxo-2H-pyridazines are starting compounds for preparation of pesticidally active compounds [1—5]. In the previous paper we have described the preparation, spectral properties, and pesticidal activity of some derivatives of 2-substituted 4,5-dichloro-3-oxo-2H--pyridazines [6]. The present paper provides the results of kinetic measurements of hydrolysis of 2-substituted 4,5-dichloro-3-oxo-2H-pyridazines utilizable in optimalization of preparation of 2-substituted 4-chloro-3-oxo-2H-pyridazin--5-ols, important intermediates in preparation of pesticidally active compounds [7—10]. The course of hydrolysis of 2-R-4,5-dichloro-3-oxo-2H-pyridazines is illustrated in Scheme 1.

Though the systems involved are polyfunctional, the results of this and other works [10, 11] show that in the case of 2-R-4,5-dihalo-3-oxo-2H-pyridazines only the halogen in position 5 manifests high reactivity towards nucleophilic
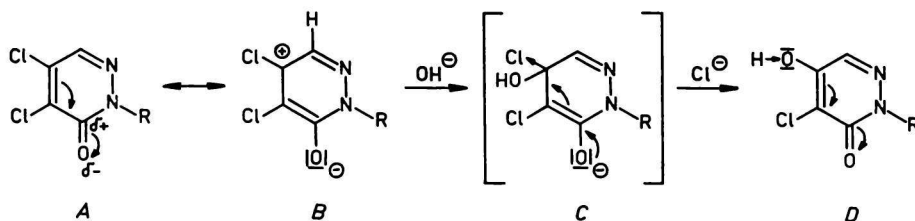
Scheme 1

reagents. Distribution of π-electrons, illustrated by mesomeric formulas A, B, indicates that nucleophilic reaction may proceed *via* the unstable form C under formation of D. In the case of the examined alkaline hydrolysis, after addition of OH^-, from the adduct C Cl^- is split off and the advantageous system of conjugated bonds is restored. Conversion of the structure A to B is influenced (beside other factors) by the $\delta +$ charge on the carbonyl carbon, and this by the nature of the substituent (R) on the vicinal nitrogen. The higher the $\delta +$, the more readily will the system react. Accordingly, the effect of the primary (derivatives I, VI, X, XII, XIV), secondary (derivative XI), and tertiary (derivative $XIII$) alkyls, bound on nitrogen in position 2, was shown to be different (Table 1). At the same conditions, hydrolysis will proceed most slowly in the

Table 1

Rate constants of hydrolysis of 2-R-4,5-dichloro-3-oxo-2H-pyridazines in alkaline medium
$c_0(NaOH) = 0.1$ mol dm^{-3}, c_0(2-R-4,5-dichloro-3-oxo-2H-pyridazine) $= 0.05$ mol dm^{-3}

Compound	R	$\theta/°C$	$10^3 k/(\text{mol dm}^{-3}\,\text{s}^{-1})$	$4 + \log k$
I	CH_3	100.0	49.10*	2.6911
II	CH_3	80.0	3.55	1.5502
III	CH_3	70.0	1.14	1.1461
IV	CH_3	60.0	0.39	0.5911
V	CH_3	50.0	0.14	0.1461
VI	C_2H_5	100.0	5.01*	1.6998
VII	C_2H_5	80.0	1.14	1.0569
$VIII$	C_2H_5	70.0	0.51	0.7076
IX	C_2H_5	60.0	0.20	0.3010
X	C_3H_7	100.0	2.78	1.4440
XI	$(CH_3)_2CH$	100.0	1.52	1.1718
XII	C_4H_9	100.0	0.80	0.9053
$XIII$	$(CH_3)_3C$	100.0	0.71	0.8513
XIV	C_5H_{11}	100.0	0.33	0.5224
XV	C_6H_{11}(cyclo)	100.0	0.24	0.3802
XVI	C_6H_5	100.0	0.93	0.9685
$XVII$	C_6H_5—CH_2	100.0	0.78	0.8921
$XVIII$	3-CH_3—C_6H_4—CH_2	100.0	0.42	0.6232

* Calculated values of rate constants.

case of *tert*-butyl, which brings about the most effective decrease in deficit of electrons ($\delta+$) on the carbonyl carbon. Nonreactivity of chlorine in position 4 of the product *D* is not surprising as the product *D* contains a strongly acid OH group and, therefore, reacts immediately with one equivalent of sodium hydroxide to give the anion of the respective salt (Scheme 2). It is evident from the
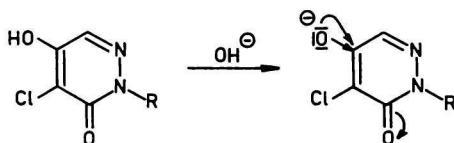
Scheme 2

structure of this anion that chlorine in position 4 is not ready to enter a further substitution. Indeed, the study of kinetics of hydrolysis confirmed the consumption of two equivalents of sodium hydroxide. The fact mentioned above was verified with the cyclohexyl derivative (compound *XV*). The rate constants of hydrolysis at various excessive amounts of sodium hydroxide in the reaction mixture (10- and 20-fold), comparable within the limits of experimental error, point to the fact that the hydroxide anion enters the reaction as a substrate. It was confirmed also by the fact that when the mole ratio of NaOH and compound *XV* was 1 : 1 the reaction proceeded at *ca.* 40 % only.

An alternate mechanism of substitution of chlorine with ring-opening, subsequent substitution of chlorine, and ring-reclosure is improbable because, as found by *Maki* and *Takaya* [11, 12], ring-opening with this type of compounds (2-phenyl-4,5-dichloro-3-oxo-2*H*-pyridazine) takes place at drastic conditions (large excess of sodium hydroxide and 130 °C) and, what is important, the reclosed ring is five-membered. In accordance with the suggested mechanism, the order of the reaction is 2.

In order to explain the reactivity of chlorines, bound in positions 4 and 5 of the studied system, the charges on chlorine-containing carbons were computed by the CNDO/2 semiempirical quantum-chemical method [13]. The geometry used was that found experimentally from roentgenographic data [14]. As seen from the data in Fig. 1, the carbon C-5 is predicted for the attack with such hard nucleophile as the hydroxyl anion, which is in agreement with the experiment.

Experimental

2-Substituted 4,5-dichloro-3-oxo-2*H*-pyridazines were prepared according to [6]. Sodium hydroxide, anal. grade, was obtained from Lachema, Brno.

Kinetic measurements

Into a three-necked flask (250 cm³), equipped with a stirrer, thermometer, and reflux and placed in a bath with thermostatic control (the error in temperature measurement was ± 0.5 °C), aqueous solution of sodium hydroxide of known concentration was added and heated to the chosen temperature under stirring. At this temperature a certain
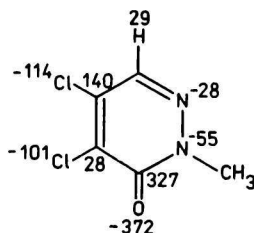

Fig. 1. Charge densities of 2-methyl-4,5-dichloro-3-oxo-2H-pyridazine ($Q \cdot 10^3$).

amount of 2-R-4,5-dichloro-3-oxo-2H-pyridazine was added to the solution. Then at time intervals samples (≤ 1 % of total volume) were withdrawn from the reaction mixture. The sample was immediately diluted with distilled water and the content of chloride anion in the solution was determined by the standard argentometric method.

The order of the reaction was calculated by the integral method according to [15]. The rate constant was calculated graphically from the dependence of the concentration increment of the chloride anion in solution at the given temperature according to the relationship

$$\frac{1}{a-x} \log \frac{a(b-x)}{b(a-x)} = kt$$

where a and b are initial concentrations (in mol dm⁻³). The correlation coefficient of rate constant in computer processing was ≥ 0.99. The rate constant value was established from three independent measurements. The relative error of determination of rate constant was ≤ 7 %. The rate constants for R = CH₃ and R = C₂H₅ at 100 °C were calculated on the basis of measured values of rate constants at temperatures 50 °C, 60 °C, 70 °C, and 80 °C from the graphical relationship $\log k = f(1/\theta)$ and are presented in Table 1. The values of activation energy (Table 2) were determined from the dependence of logarithm of rate constant on the reciprocal value of absolute temperature according to the Arrhenius equation [15]

$$k = A e^{-E_A/RT}$$

The error of activation energy was calculated from the relationship [15]

$$\Delta E_A = \frac{R T_1 T_2}{T_2 - T_1} \left[\left(\frac{\Delta k_1}{k_1} \right)^2 + \left(\frac{\Delta k_2}{k_2} \right)^2 \right]^{1/2}$$

where Δk_1 and Δk_2 are the average errors of the rate constant. The value of the error of

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Table 2

Activation parameters of hydrolysis of 2-R-4,5-dichloro-3-oxo-2*H*-pyridazines in alkaline medium
$c_0(NaOH) = 0.1 \text{ mol dm}^{-3}$, $c_0(2\text{-R-4,5-dichloro-3-oxo-2}H\text{-pyridazine}) = 0.05 \text{ mol dm}^{-3}$

Compound	R	$E_A/(\text{kJ mol}^{-1})$	$\Delta S^+/(\text{J mol}^{-1}\text{ K}^{-1})$
I	CH_3	102.7	141
II	C_2H_5	95.8	152

activation energy does not exceed $\pm 10\%$. The values of activation entropy (Table 2) were determined from the relationship [16]

$$S = R \ln (Ah/kTe)$$

where A is the preexponential factor of the Arrhenius equation, k is the Boltzman constant, e is the base of natural logarithms, h is the Planck constant, and T is absolute temperature.

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