

## KINETICS OF THE REACTION OF GUANYL-O-METHYLISOUREA HYDROCHLORIDE WITH DIMETHYLFORMAMIDE DIMETHYLACETAL

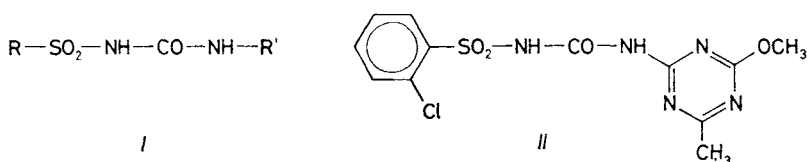
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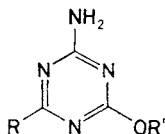
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The reaction of guanyl-O-methylisourea hydrochloride (*IV*) with dimethylformamide dimethylacetal (*V*) proceeds in two steps. The first step consists in the reaction of the imidoester with the imidatonium ion formed in a fast pre-equilibrium to give a conjugated system with the absorption maximum at 278 nm. The subsequent slower step consists in the cyclization to 2-amino-4-methoxy-1,3,5-triazine (*VI*). The rate of the first step is directly proportional to the concentrations of both hydrochloride *IV* and acetal *V*. Both the steps involve base catalysis. Mechanism of the whole reaction is suggested on the basis of the kinetic results.

The herbicides which attract the greatest attention at present contain active components based on sulphonylated ureas type *I* prepared by addition of amines  $R'NH_2$  to sulphonylisocyanates  $RSO_2NCO$  (ref.<sup>1</sup>). The amines  $R'NH_2$  most usually contain a five-membered heterocyclic residue<sup>2</sup> or a six-membered one with one<sup>3</sup>, two<sup>4-7</sup>, or three heteroatoms<sup>5,8-10</sup>. This group of compounds also includes 1-(2-chlorophenylsulphonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea (*II*), which is produced as a so-called 3<sup>rd</sup>-generation selective herbicide under commercial names DPX 4189 or Glean<sup>11,12</sup>.

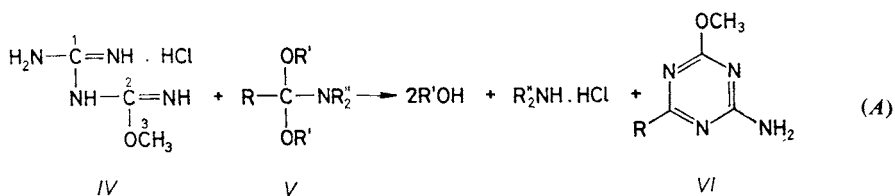


The main problem of syntheses of this type of herbicides lies in the preparation of the substituted triazines type *III*



*III*, R = H, alkyl; R' = alkyl

One of the ways to preparation of compounds *III* consists in the cyclization of guanyl-O-methylisourea hydrochloride (*IV*) with *N,N*-dialkylamide acetals (reaction (*A*)).



The aim of the present work is a study of the cyclization reaction of hydrochloride *IV* with dimethylformamide dimethylacetal (*V*) giving 2-amino-4-methoxy-1,3,5-triazine (*VI*).

## EXPERIMENTAL

*Syntheses of the compounds.* Guanyl-O-methylisourea hydrochloride (*IV*) was prepared by addition of methanol to dicyandiamide catalyzed with hydrogen chloride<sup>13,14</sup> with the yield of 23%, m.p. 156–157°C (ethanol). Structure of the compound was verified by <sup>13</sup>C NMR spectra:  $\delta_1 = 162.57$  (a singlet in the proton coupled spectrum),  $\delta_2 = 159.06$  (quartet,  $^3J_{\text{CH}} = 4.4$  Hz),  $\delta_3 = 54.93$  (quartet,  $^1J_{\text{CH}} = 148.0$  Hz). Dimethylformamide dimethylacetal (*V*) was prepared by methylation of dimethylformamide with dimethyl sulphate and subsequent reaction of the intermediate with methoxide according to a known procedure<sup>15</sup> in the yield of 75%, m.p. 102–103°C. 2-Amino-4-methoxy-1,3,5-triazine (*VI*) was prepared by a reaction of compounds *IV* and *V* according to ref.<sup>14</sup> but without addition of methoxide, yield 83%, m.p. 188–189°C.

*Spectral measurements.* The electronic spectra were measured with a Specord UV VIS apparatus. The <sup>13</sup>C NMR spectra of compound *IV* were measured with a JNM-FX 100 JEOL at 25.047 MHz at 25°C in hexadeuteriodimethyl sulphoxide solution. The carbon chemical shifts (see preparation of compound *IV*) are related to internal tetramethylsilane (for numbers of the carbon atoms see formula *IV* in Eq. (*A*)).

*Kinetic measurements.* First we measured electronic spectra of the starting compounds *IV* and *V* and product *VI* in the region of 200–400 nm. Then, spectra of mixtures of compounds *IV* and *V* were measured in the same region at suitable time intervals: 1 min for the first reaction step (the increase and beginning decrease of the absorbance) and 4 min for the slower reaction (the absorbance decrease). These experiments enabled a selection of suitable wavelength (278 nm) for the proper kinetic measurements. A quartz cell ( $d = 1$  cm) with stopper was charged with 2 ml methanolic solution of the hydrochloride *IV* ( $0.005$  to  $0.1 \text{ mol l}^{-1}$ ) and placed into the thermostated cell compartment (25°C) of the spectrophotometer. After reaching the above-mentioned temperature, cyclohexane solution of the acetal *V* ( $0.2 \text{ mol l}^{-1}$ ) was added so that its concentrations in the reaction mixture were  $5 \cdot 10^{-4}$  to  $1 \cdot 10^{-3} \text{ mol l}^{-1}$ . Then the time dependence of absorbance (at first its increase and then decrease) was measured at 278 nm. In the experiments exhibiting a sufficiently large difference between the rate constants of the first and the second reaction steps, a certain amount (20–200  $\mu\text{l}$ ) of  $0.1 \text{ mol l}^{-1}$  sodium methoxide

solution was added to the solution of compound *IV*. In a next experimental series, the solutions of compounds *IV* and *V* were mixed and, after the maximum absorbance was crossed, 20–200  $\mu\text{l}$  of  $0.1 \text{ mol l}^{-1}$  methoxide or  $1 \text{ mol l}^{-1}$  triethylamine in methanol was added into the cell. The rate constant of the subsequent reaction was calculated from the absorbance decrease. Fig. 1 presents a typical record of the kinetic experiment. The rate constant of the slower reaction step ( $k_2$ ) was calculated from the decreasing section of the curve according to Eq. (1)

$$k_2 t = -2.303 \log (A_t - A_\infty), \quad (1)$$

where  $A_t$  and  $A_\infty$  stand for the absorbance at the time  $t$  and after six halfives, respectively. The rate constant of the faster reaction step ( $k_1$  in Eq. (2)) was calculated from the time dependence of logarithm of differences of the absorbances of the slower reaction step extrapolated to the time  $t = 0$  ( $A_{\text{extrap}}$ ) and the absorbances  $A_t$  measured using the procedure of ref.<sup>16</sup>.

$$k_1 t = -2.303 \log (A_{\text{extrap}} - A_t) \quad (2)$$

TABLE I

The rate constants  $k_1$  and  $k_2$  ( $\text{s}^{-1}$ ) of the consecutive reactions  $IV + V \xrightarrow{k_1} VII \xrightarrow{k_2} VI$  (methanol,  $25^\circ\text{C}$ ) at various initial concentrations ( $\text{mol l}^{-1}$ ) of hydrochloride *IV* ( $[V]_0 = 5 \cdot 10^{-4}$  to  $1 \cdot 10^{-3} \text{ mol l}^{-1}$ )

$10^2 \cdot [IV]_0$	$10^2 \cdot k_1$	$10^3 \cdot k_2$
0.5	0.525	1.63
1	0.805	1.83
2	1.27	2.08
3	1.45	2.25
4	2.1	2.30
5	2.55	2.33
7	3.15	2.33
10	4.65	2.50

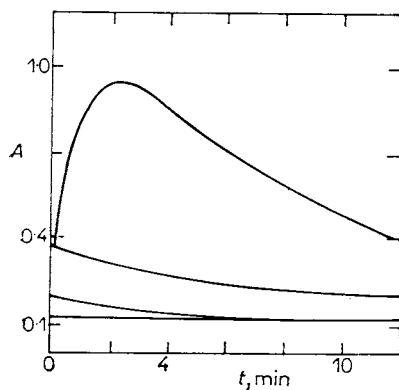


FIG. 1

Absorbance changes ( $\lambda = 278 \text{ nm}$ ,  $d = 1 \text{ cm}$ ) with time in the reaction  $IV + V \rightarrow VII \rightarrow VI$  in methanol at  $25^\circ\text{C}$  ( $[IV]_0 = 4 \cdot 10^{-2} \text{ mol l}^{-1}$ ,  $[V]_0 = 7 \cdot 10^{-4} \text{ mol l}^{-1}$ ). The time interval between the end of one curve and the beginning of the next one is always 1 min

Tables I–III give the concentrations of compound *IV* and the bases added in the individual kinetic runs along with the rate constants measured. All the experiments were carried out twice, and if the values obtained differed by more than 10%, the experiment was repeated once more.

## RESULTS AND DISCUSSION

From the spectral records of the kinetic runs it was found that the reaction is connected with a rapid initial absorbance increase at 278 nm followed by a slower decrease. This means that the cyclization  $IV + V \rightarrow VI$  proceeds kinetically as

TABLE II

The rate constants  $k_1$  and  $k_2$  ( $s^{-1}$ ) of the consecutive reactions  $IV + V \xrightarrow{k_1} VII \xrightarrow{k_2} VI$  (methanol, 25°C) at various initial concentrations ( $\text{mol l}^{-1}$ ) of sodium methoxide ( $[IV]_0 = 1 \cdot 10^{-1} \text{ mol l}^{-1}$  and  $5 \cdot 10^{-2} \text{ mol l}^{-1}$  for the column<sup>a</sup> and columns<sup>b</sup>, respectively)

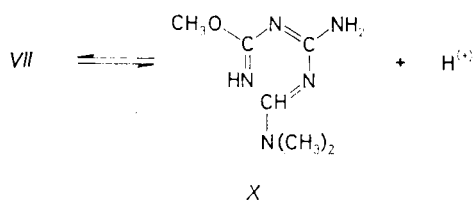
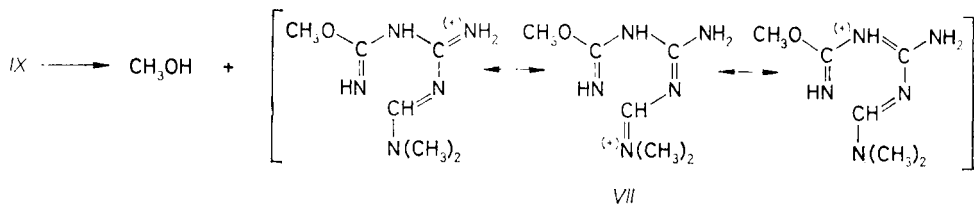
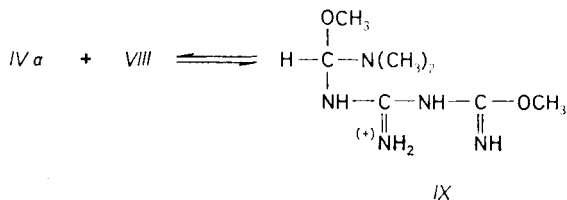
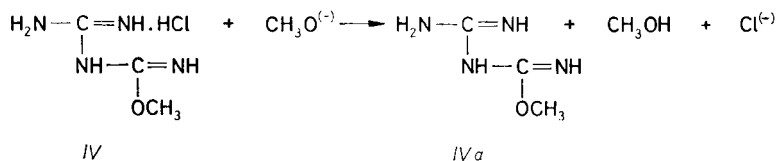
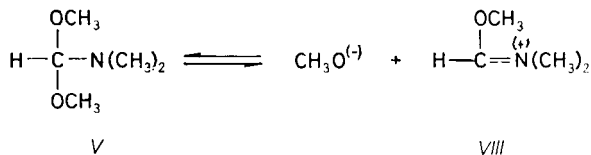
	$10^3 \cdot [\text{CH}_3\text{O}^{(-)}]$	$10^2 \cdot k_1^b$	$10^2 \cdot k_2^a$	$10^2 \cdot k_2^b$
	0	2.8	0.25	0.22
	1	9.0	0.35	0.74
	2	15.0	0.70	1.95
	3	18.5	1.1	5.8
	4	23.0	1.5	6.6
	5	—	2.7	—
	6	—	4.1	—
	7	—	7.0	—
	8	—	8.8	—

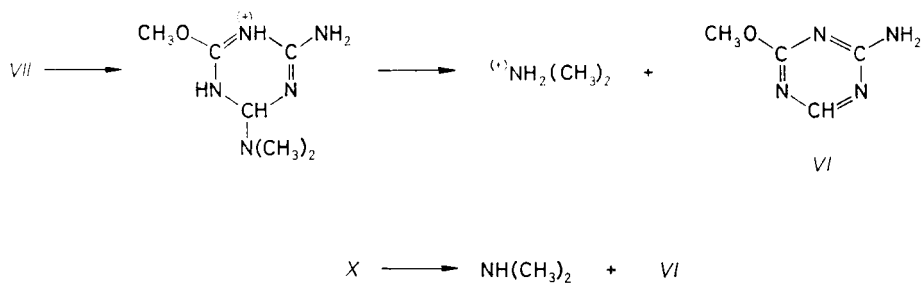
TABLE III

The rate constants  $k_2$  ( $s^{-1}$ ) of the second step of the reaction sequence  $IV + V \xrightarrow{k_2} VI$  (methanol, 25°C,  $[IV]_0 = 1 \cdot 10^{-1} \text{ mol l}^{-1}$ ) at various concentrations ( $\text{mol l}^{-1}$ ) of triethylamine

	$10^2 \cdot k_2$	$10^2 \cdot [\text{N}(\text{C}_2\text{H}_5)_3]$
	1.5	1
	3.0	2
	4.6	3
	6.0	5
	10.0	10

a two-step reaction. We suppose that the intermediate with the absorbance maximum at 278 nm has the structure *VII*, ref.<sup>17</sup> (see Scheme 1). The kinetic experiments proper were followed at this wavelength and the record (Fig. 1) is typical for a system of consecutive competitive reactions. Dependences of both the rate constants on the





SCHEME 1

substrate *IV* concentration were determined. The rate constant of the faster reaction increased linearly with increasing concentration of the hydrochloride *IV* (Table I), and, at the same time, the maximum absorbance and, hence, also the concentration of the intermediate *VII* were increased. Therefrom it follows that the higher rate constant corresponds to the formation of the intermediate *VII*, i.e. to the first reaction step. The linear dependence of the rate constant of the first reaction step on the concentration of the hydrochloride *IV* (Table I) corresponds to the kinetic equation (3). There are two possible interpretations of Eq. (3): The rate-limiting step

$$v = k_1[\text{IV}][\text{V}] \quad (3)$$

of formation of the intermediate *VII* consists in the reaction of acetal *V* with the protonated amine *IV*, the formation of the cation *VIII* being subject to general acid catalysis. The other possibility presumes a rapid pre-equilibrium ( $\text{V} \rightleftharpoons \text{CH}_3\text{O}^{(-)} + \text{VIII}$ ) strongly shifted to the left. The rate-limiting step then consists in a reaction of the carbenium ion *VIII* with the liberated amine *IVa* or in some of the subsequent steps. In this case the reaction rate is given by Eq. (4)

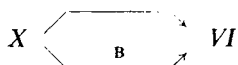
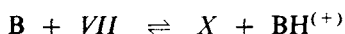
$$v = k_1[\text{VIII}][\text{IVa}] = kK[\text{V}][\text{IV}], \quad (4)$$

where *K* means the equilibrium constant of the pre-equilibrium.

The results in Table II show that the rate constant  $k_1$  of the first step increases with increasing methoxide concentration and, hence, also with that of the liberated amine *IVa*. So the reaction is base catalyzed, which excludes the first interpretation (the acid-catalyzed formation of the carbenium ion *VIII* in the rate-limiting step). The value of the product  $[\text{VIII}][\text{IVa}]$  depends on the product  $[\text{V}][\text{IV}]$ . Thus it does not practically depend on the amount of amine *IVa* formed after the addition of methoxide, because increasing concentration of amine *IVa* causes proportional

decrease of the amount of the carbenium ion *VIII* in the reaction mixture\*. The effect of the liberated amine *IVa* on the rate constant cannot make itself felt until in the subsequent reaction of the primary intermediate *IX* which involves splitting off of methoxy group and proton to give the intermediate *VII* with a longer conjugated chain absorbing at 278 nm.

The rate constant  $k_2$  of the second (slower) step increases at first with the first power and then with the square of methoxide concentration, the value of the exponent being again decreased at the highest alkoxide concentrations. This decrease of exponent is accompanied by a decrease of absorbance of the protonated intermediate *VII*, which means that the protonated intermediate *VII* is transformed into neutral compound *X* which does not absorb at the wavelength of 278 nm. The base (B) can operate in three ways, as it is shown in Scheme 2. The quadratic dependence would correspond to the base-catalyzed transformation  $X \xrightarrow{B} VI$ .



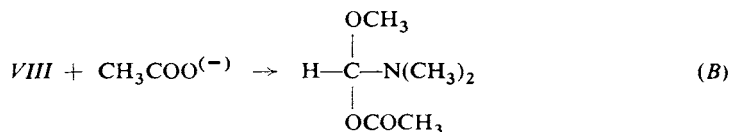
SCHEME 2

The pH dependence of the rate constant  $k_2$  of the second step is confirmed by the finding that with a half concentration of the hydrochloride *IV* a comparable change in  $k_2$  is obtained with addition of half amount of methoxide (except for the highest methoxide concentrations, when the general base catalysis is manifested most markedly).

In several experiments we followed the effects of triethylamine and acetate ion on the rate of the second reaction step (*VII*  $\rightarrow$  *VI*). In the case of triethylamine, the rate constant increased linearly with its concentration at the beginning. At higher triethylamine concentrations, the value of the exponent decreased and, at the same time, the absorbance of intermediate *VII* decreased almost to one half of the original value. The decrease in the exponent is obviously caused by concentration decrease of the protonated intermediate *VII* (due to its dissociation to the neutral base *X*). Acetate ion had no effect on the rate constant of the second reaction step in accordance with the fact that acetate is by several orders of magnitude weaker base than the two amines (triethylamine and compound *IVa*). It was surprising to find that addition of acetate immediately at the beginning of the reaction caused but

\* The concentration decrease of hydrochloride *IV* after addition of methoxide is practically negligible with respect to the error connected with determination of  $k_1$ .

a slight absorbance increase due to formation of the intermediate *VII*. One of possible explanations consists in the attack of carbenium ion *VIII* by acetate anion (reaction (B)) with the equilibrium



strongly shifted in favour of the products. Thereby the rate of formation of intermediate *VII* would be strongly decreased, the rate constant  $k_2$  of the transformation  $VII \rightarrow VI$  remaining the same.

## REFERENCES

1. Levitt G.: Ger. 2715786; Chem. Abstr. 88, 6935 (1978).
2. Du Pont: Europ. pat. 73562; Central Patents Index, Section C, Week 11, 1983.
3. Du Pont: U. S. 4372778; Central Patents Index, Section C, Week K08, Y983.
4. Levitt G.: Braz. Pedido PI 7806086; Chem. Abstr. 92, 76548 (1980).
5. Levitt G.: Europ. pat. 13480; Chem. Abstr. 94, 83952 (1981).
6. Sauer R. F.: Europ. pat. 51466; Chem. Abstr. 98, 16731 (1983).
7. Nissan Chemical Industries: Japan. Kokai 58162587; Chem. Abstr. 100, 139151 (1984).
8. Levitt G.: U.S. 4225337; Chem. Abstr. 95, 43175 (1981).
9. Schwing G. W., Woods T. S.: Europ. pat. 24215; Chem. Abstr. 95, 80222 (1981).
10. Levitt G.: Europ. pat. 30142; Chem. Abstr. 95, 150713 (1981).
11. Palm H. L., Riggleman J. D., Allison D. A.: *Proc. Br. Crop. Prof. Conf. Weeds 1980*, 15 (1), 1; Chem. Abstr. 95, 56104 (1980).
12. Aamisepp A.: *Weeds, Weed Control* 22, 1 (1981); Chem. Abstr. 94, 203710 (1981).
13. Kawano A., Odo K.: *Nippon Kagaku Zasshi* 82, 1672 (1961); Chem. Abstr. 58, 11212 (1963).
14. Piskala A.: *This Journal* 32, 3966 (1967).
15. Arnold Z., Kornilov M.: *This Journal* 29, 645 (1964).
16. Jackson W. G., Harrowfield J. M., Vowles P. D.: *Int. J. Chem. Kinet.* 9, 535 (1977).
17. Kuhn H.: *Fortschr. Chem. Org. Naturst.* 16, 169 (1958).

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