SOLVOLYSIS KINETICS AND MECHANISM OF 3-METHYL-1,3-THIAZOLIDINE-2,4-DIONE

Vladimír MACHÁČEK, Vojeslav ŠTĚRBA and Helena ZAHRADNÍČKOVÁ

Department of Organic Chemistry,
Institute of Chemical Technology, 53210 Pardubice

Received January 21st, 1981

The hydrolysis kinetics of 3-methyl-1,3-thiazolidine-2,4-dione have been studied in aqueous buffers and dilute NaOH solutions. The reaction proceeds *via* two base-catalyzed steps having different rates. In sodium methoxide solutions 3-methyl-1,3-thiazolidine-2,4-dione undergoes one-step methanolysis giving methyl thioglycolate anion as the final product. The rate-limiting step consists in decomposition of the anion $CH_3\overline{N}COSCH_2COOCH_3$.

N-Substituted 1,3-thiazolidine-2,4-diones are efficient fungicides[1] and plant growth stimulants[2]. An important criterion of practical applicability of biologically active substances is their stability in aqueous medium and dependence of hydrolysis rate on pH. In this work the hydrolysis kinetics of 3-methyl-1,3-thiazolidine-2,4-dione (*I*) is studied in aqueous buffers, and the methanolysis kinetics of *I* is studied in sodium methoxide solutions.The methanolysis intermediate – S-(methoxycarbonylmethyl)-N-methylthiocarbamate anion (*II*) – can either be cyclized back to the dione *I* or split off methyl isocyanate. In order to estimate which of the two reactions proceeds faster, we also studied reactions of the separately prepared *II* in methanolic methoxide.

EXPERIMENTAL

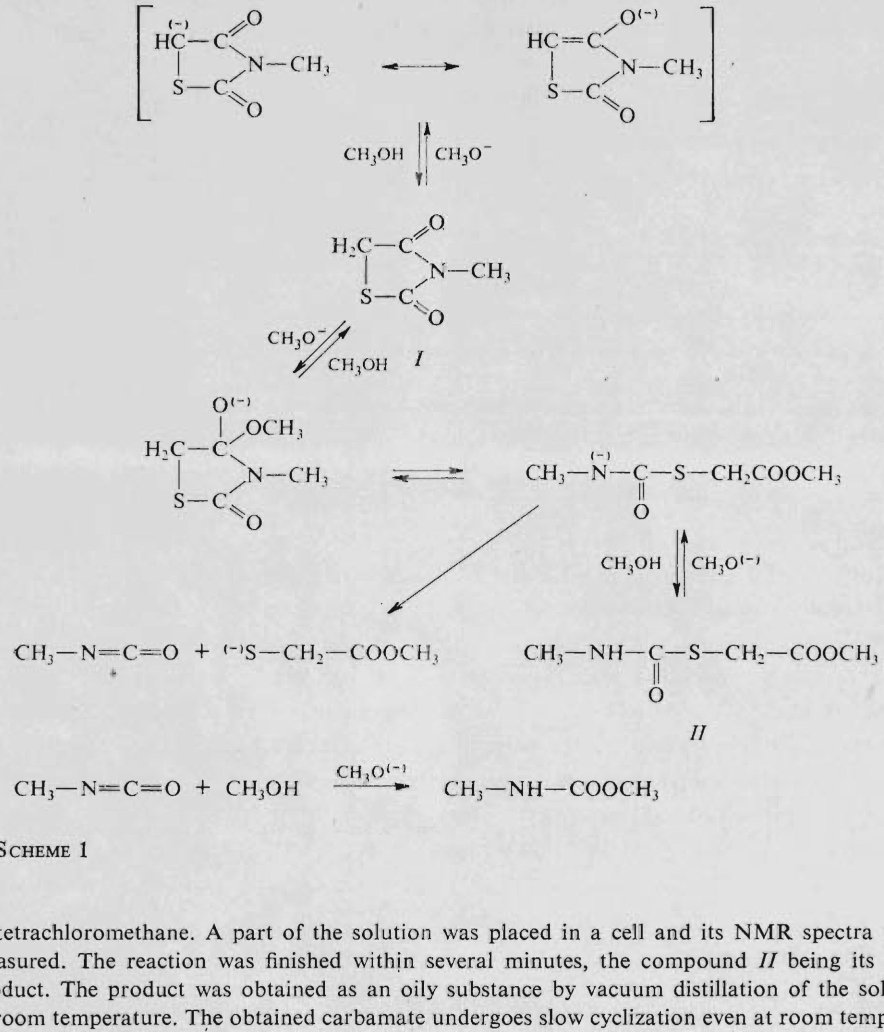
The ^{1}H-NMR spectra were measured with a Tesla BS 487 B apparatus at 80 MHz using hexamethyldisiloxane as internal standard.

The pH values of the reaction solutions were obtained with a Radiometer pHm 4c apparatus using a combined glass and calomel electrode.

3-Methyl-1,3-thiazolidine-2,4-dione was prepared by heating solution of 9 g (0·1 mol) N-methylthiourea and 9·4 g (0·1 mol) chloroacetic acid in 40 ml water on boiling water bath for 48 h. The raw product was extracted in chloroform and purified by vacuum distillation. Yield 73%, m.p. 39—41°C (ref.[3] m.p. 40·5—41·5°C). Methyl thioglycolate was prepared by azeotropic esterification and purified by vacuum distillation under nitrogen.

S-(Methoxycarbonylmethyl)-N-methylthiocarbamate (*II*)

Solution of 1·06 g (10 mmol) methyl thioglycolate in 10 ml tetrachloromethane was treated with 0·68 g (12 mmol) methyl isocyanate and 1 drop of about 10% solution of triethylamine



SCHEME 1

in tetrachloromethane. A part of the solution was placed in a cell and its NMR spectra were measured. The reaction was finished within several minutes, the compound *II* being its only product. The product was obtained as an oily substance by vacuum distillation of the solvent at room temperature. The obtained carbamate undergoes slow cyclization even at room temperature, therefore a fresh product was used for each kinetic measurement. ^{1}H NMR spectrum (CCl_4, 25°C): $\delta(OCH_3) = 3{\cdot}71$ (singlet, 3 H), $\delta(NH) = 6{\cdot}84$ (broadened quartet, 1 H), $\delta(CH_2S) = 3{\cdot}65$ (singlet, 2 H), $\delta(CH_3N) = 2{\cdot}84$ (doublet, 3 H, $^3J = 4{\cdot}5$ Hz).

Kinetic Measurements

The kinetic measurements were carried out with a Zeiss VSU 2P apparatus at 25°C. For kinetic study of hydrolysis of the dione *I* (the first reaction step) 2 ml carbonate buffer solution ($I = 0{\cdot}5$) was placed in a 10 mm quartz cell, and one drop of $2 \cdot 10^{-2}$ mol l^{-1} methanolic solution of the dione *I* was added thereto, whereupon time dependence of absorbance was measured at 240 nm. The rate constants k_{obs} were calculated from the equation $k_{obs} \cdot t = -2{\cdot}303 \log (A_\infty - A_t) + \text{const.}$ At higher buffer concentrations consecutive reactions made themselves felt, and, therefore, the A_{∞} values had to be corrected by linear extrapolation, Rate of the second hydrolysis step of the dione *I* was followed in the same way in aqueous NaOH solutions.

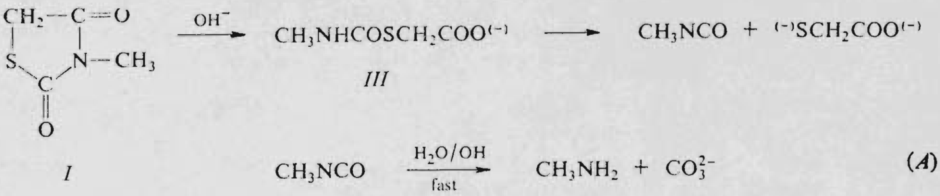
Methanolysis of the dione *I* was followed in sodium methoxide solutions: 2 ml $7{\cdot}2 \,.\, 10^{-3}$ to $1{\cdot}96$ mol l^{-1} methoxide solution was placed in 10 mm quartz cell and treated with one drop $2 \,.\, 10^{-2}$ mol l^{-1} methanolic solution of the dione *I*, whereupon the absorbance increase was measured at 255 nm. The rate constants were calculated in the same way.

Kinetics of cyclization of thiocarbamate *II* to the dione *I* was measured in the same way as the above-mentioned reactions using phosphate buffers at 232 nm at $I = 0{\cdot}5$ and butylamine-butylamonium chloride buffers in methanol at 240 nm. The rate constants k_{obs} were calculated in the same way.

RESULTS AND DISCUSSION

The base-catalyzed hydrolysis of 3-methyl-1,3-thiazolidine-2,4-dione (*I*) proceeds in two kinetically separated steps (Eq. (*A*)).*

Rate of the first step (opening of the thiazolidine cycle) was measured in carbonate buffers within the pH range 9·80–10·20. The reaction proceeded as pseudomonomolecular reaction. Increasing concentration of carbonate ion had the consequence that subsequent decomposition of anion of S-(methylaminocarbonyl)thioglycolic acid (*III*) became increasingly singnificant, which was manifested by increasing absorbance values after 4–6 half-lives of the first hydrolysis step (depending on CO_3^{2-} concentration).



(*A*)

Rate of opening of thiazolidine cycle was independent of the buffer concentration at the given pH value (general base catalysis did not operate), and the k_{obs} values increased linearly with increasing activity of hydroxyl ion (Eq. (*1*), Table I).

$$v = k \,.\, a_{OH} \cdot [I] = k_{obs} \cdot [I] \qquad (1)$$

The reaction is first order in OH^- and exhibits specific base catalysis, which indicates that the rate-limiting step of the ring opening consists in attack of hydroxyl ion on the carbonyl carbon atom $C_{(4)}$ (similar to the base-catalyzed hydrolysis of 3-aryl-1,3-diazolidine-2,4-diones described in ref.[4]). However, in contrast to the

---

* Electronic spectrum of the intermediate formed during hydrolysis of the dione *I* is very similar to that of thiocarbamate *II*, especially so after acidification of the reaction mixture.

thiazolidinedione *I*, the primary hydrolysis product of 3-aryl-1,3-diazolidine-2,4-dione (*i.e.* N'-arylureido acetate ion) is stable in aqueous alkali medium and represents the final reaction product.

Kinetics of the second hydrolysis step of the dione *I* (decomposition of anion of the acid *III*) was studied in dilute NaOH solutions. At the NaOH concentrations used the dione *I* undergoes rapidly the ring opening, hence it is not present in the reaction mixture even during the first absorbance measurement (*i.e.* about 20 s after the reaction start). Spectrum of the reaction mixture after finishing the reaction was identical with that of thioglycolic acid dianion. Absorbance of these solutions changed with time due obviously to oxidation of the thioglycolic acid dianion. After correction of A_∞ with respect to this change the found time dependences of log $(A_\infty - A_t)$ were linear up to at least 3 half-lives, which means that the reaction had pseudomonomolecular course. The rate constants k_{obs} of the second hydrolysis step of the dione *I* increase with increasing concentration of hydroxyl ion (Table II), but the reaction order with respect to OH^- concentration is substantially higher than unity.

TABLE I

Rate constants of opening of 3-methyl-1,3-thiazolidine-2,4-dione cycle in aqueous carbonate buffers at 25°C ($I = 0{\cdot}5$)

$[KHCO_3]$	$[K_2CO_3]$	pH	$k_{obs} \,.\, 10^3$, s^{-1}	k_2, $l\ mol^{-1}\ s^{-1}$ [a]
0·08	0·04	9·80	1·18	18·7
0·04	0·04	9·97	1·89	20·2
0·06	0·06	10·04	2·04	18·5
0·10	0·10	10·05	2·06	18·2
0·02	0·04	10·20	3·16	19·9

[a] $k_2 = k_{obs}/a_{OH^-}$; $\bar{k}_2 = (19{\cdot}1 \pm 1{\cdot}8)\ l\ mol^{-1}\ s^{-1}$.

TABLE II

Rate constants of the second step of hydrolysis of 3-methyl-1,3-thiazolidine-2,4-dione (*I*) in aqueous NaOH solutions at 25°C ($I = 0{\cdot}5$)

$[OH^-]$	0·02	0·01	0·005
$k_{obs} \,.\, 10^3$, s^{-1}	12·7	4·81	1·50

The methanolysis of the dione *I* was a kinetically one-step reaction. After the finished reaction spectrum of the reaction mixture was identical with that of methylthioglycolate anion. The methanolysis course can be represented by Scheme 1. The reaction was pseudomonomolecular in the whole course. At lower methoxide concentrations (below 0·5 mol l^{-1}) the found rate constants increased linearly with increasing methoxide concentration. At higher sodium methoxide concentrations the increase of k_{obs} was slower than that of methoxide concentration. Dependence of log k_{obs} on the acidity function H_M (ref.[5]) is represented in Fig. 1. The deviation from linearity is due to dissociation of 3-methyl-1,3-thiazolidine-2,4-dione into its anion

TABLE III

Cyclization rate constants of S-(methoxycarbonylmethyl)-N-methylthiocarbamate (*II*) in methanolic butylamine-butylamonium chloride buffers at 25°C

$[C_4H_9NH_2]$	$[C_4H_9\overset{(+)}{N}H_3Cl^-]$	k_{obs} . 10^3, s^{-1} [a]
0·1	0·01	3·25[b]
0·02	0·01	6·42[b]
0·04	0·01	13·12[b]
0·005	0·01	1·83[b]
0·02	0·01	8·88[c]
0·04	0·02	10·27[c]
0·06	0·03	10·50[c]
0·08	0·04	11·27[c]

[a] $\bar{k} = k_{obs}/[CH_3O^-] = (5·5 \pm 0·5) . 10^2 \ l \ mol^{-1} \ s^{-1}$ for $I = 0·01$; [b] $I = 0·01$; [c] $I = 0·04$.

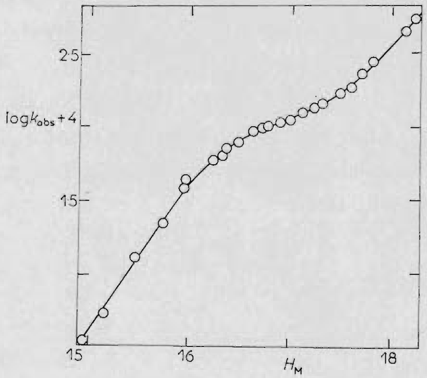


FIG. 1

Dependence of logarithm of the methanolysis rate constant k_{obs} of 3-methyl-1,3-thiazolidine-2,4-dione (*I*) on the H_M acidity function

(Scheme 1). From the dependence in Fig. 1 it can be seen that the dione *I* has pK_a about 16·6 (as C-acid). At the H_M values above 17·5 almost all the dione *I* is present in the form of the anion, and the observed rate constant k_{obs} should not increase with increasing H_M value. The found increase of k_{obs} can be explained by different influence of medium on activity coefficients of the conjugated base of the dione *I* and the activated complex of the rate-limiting step. The bimolecular rate constant of methanolysis of the dione *I* calculated from linear section of the dependence log k_{obs} *vs* H_M is $k = (4{\cdot}8 \pm 0{\cdot}2) \,.\, 10^{-2}\, l\, mol^{-1}\, s^{-1}$.

The rate-limiting step of the methanolysis can consist either in opening of the thiazolidine cycle or in splitting of the primary intermediate $CH_3\overset{(-)}{N}COSCH_2COOCH_3$ into products. For unambiguous estimation of the rate-limiting step we prepared the intermediate *II* by an independent synthesis and studied its reactions with bases. In diluted methanolic sodium methoxide the intermediate *II* was immediately cyclized into the dione *I*, whereupon the methanolysis products were slowly formed (the reaction course was followed with a Unicam SP 800 spectrophotometer). This fact indicates that the cyclization rate of anion of the intermediate *II* is much greater than its splitting rate, and the rate-limiting step of methanolysis of the dione *I* consists in splitting of the anion $CH_3\overset{(-)}{N}COSCH_2COOCH_3$.

The cyclization rate of the intermediate *II* in methanol was measured with butylamine–butylammonium chloride buffers. In the whole range measured the reaction proceeded as pseudomonomolecular, the rate constant k_{obs} was (at constant ionic strength) very little dependent on the buffer concentration and increased linearly with methoxide ion activity. Using the value $pK_a = 11{\cdot}70$ for butylamonium ion in methanol[6], $pK_{CH_3OH} = 16{\cdot}916$ (ref.[7]), concentration ratio of the buffer components, and the measured rate constants k_{obs} (Table III), we calculated the bimolecular rate constant of cyclization of the compound *II* to be $\bar{k} = (5{\cdot}5 \pm 0{\cdot}5) \,.\, 10^{2}\, l\, mol^{-1}\, s^{-1}$.

The cyclization of the thiocarbamate *II* was also studied in aqueous phosphate buffers. The dione *I* was the reaction product in this case, too. The reactions had pseudomonomolecular course, the rate was directly proportional to concentration of hydroxyl ions and independent of the buffer concentration. The calculated bimolecular rate constant of the cyclization is $\bar{k} = (14{\cdot}6 \pm 1{\cdot}5) \,.\, 10^{3}\, l\, mol^{-1}\, s^{-1}$. The found cyclization rate constant of thiocarbamate *II* in water has a substantially greater value than in methanol, which is similar to cyclization of ethyl N′-arylureido-2-butenoates[8].

REFERENCES

1. Sundholm N. K., Skaptason J. B.: U.S. 2 510 725; Chem. Abstr. *44*, 8045 (1950).
2. Morel G., Memoret Y., Levy R., Gryszkiewicz-Trochimovski O.: Fr. Addn. 79 984; Chem. Abstr. *59*, 10 061 (1963); to Fr. 1 284 516; Chem. Abstr. *58*, 1463 (1962).

3. Holmberg B., Rosen W.: Chem. Ber. *58*, 1834 (1925).
4. Bergon M., Calmon J. P.: J. Chem. Soc., Perkin Trans. *2*, 1978, 493.
5. Rochester C. H.: *Acidity Functions*, p. 246. Academic Press, London 1970.
6. Ritchie C. D., Minasz R. J., Kamego A. A., Sawada M.: J. Amer. Chem. Soc. *99*, 3747 (1977).
7. Rochester C. H., Rossal B.: J. Chem. Soc. B *1967*, 743.
8. Hloušek J., Macháček V., Štěrba V.: Sb. Věd. Pr. Vys. Šk. Chemickotechnol., Pardubice *39*, 11 (1978).

Translated by J. Panchartek.