

# Kinetics and Mechanism of Mercury(II)-Catalyzed Cyclization of *N*-Phenyl-2-vinyl-2-oxazolidinamine

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**Abstract**—The kinetic and thermodynamic parameters of the Hg(II)-catalyzed cyclization of *N*-phenyl-2-vinyl-2-oxazolidinamine indicated that the first reaction step is reversible coordination of mercury at the vinyl group, followed by closure of mercurated oxazolidinone ring (the rate-determining step); the latter undergoes demercuration to give 2-methyl-3-phenyl-2-oxazolidinone either by the action of mercury salt anion or spontaneously.

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Vinyl ethers derived from glycols readily undergo acid-catalyzed cyclization to 2-methyl-1,3-dioxolanes [1]. By contrast, vinyl ethers derived from amino alcohols react with acids in a nonselective fashion due to the presence of nitrogen atom [2]. Vinyl ethers having a strongly basic nitrogen atom (amino or alkylamino groups) do not undergo cyclization in the presence of protic acids, but they sometimes give rise to open-chain salts [2, 3], while their tendency to intramolecular ring closure increases as the basicity of the nitrogen atom decreases. For example, *N*-phenyl-2-vinyl-2-oxazolidinamine (**I**) in the presence of hydrochloric acid is converted into 2-methyl-3-phenyl-2-oxazolidinone (**II**) by 13% [4], whereas even less basic vinyl ethers derived from 2-(acylamino)ethanols give rise to the corresponding oxazolidinones in quantitative yield [5].

We previously showed that 2-vinyl-2-oxazolidinamines, regardless of the basicity of the nitrogen atom, undergo cyclization into oxazolidinones by the action of soft acids such as Sn<sup>2+</sup> and Ag<sup>+</sup> [6] and especially readily (in 48 to 100% yield) in the presence of Hg<sup>2+</sup> and Pd<sup>2+</sup> [6–8]. It was presumed that, unlike hard acids which attack the nitrogen atom, soft acids coordinate mainly at the soft π-basic center (double bond), thus favoring intramolecular cyclization [2].

With a view to verify the proposed reaction mechanism, in the present work we examined the kinetics of cyclization of *N*-phenyl-2-vinyl-2-oxazolidinamine (**I**) in *N*-methylpyrrolidin-2-one as solvent by the action of

mercury(II) acetate and chloride. The choice of the substrate and catalysts was dictated by the fact that the reaction performed on a preparative scale resulted in the formation of 2-methyl-3-phenyl-2-oxazolidinone (**II**) in quantitative yield [6, 7].

The kinetic experiments were performed using the same initial concentration (1.17 M) of vinyl ether **I** in *N*-methylpyrrolidin-2-one. The reaction rate was calculated from the variation of the substrate concentration which was measured by GLC. The reaction was characterized by first order with respect to the substrate at a constant catalyst concentration. The rate constants  $k_{\text{exp}}$  at different temperatures and catalyst concentrations (see table) were calculated by the equation

$$k_{\text{exp}} = 2.303 \tau^{-1} \log(c_0/c_\tau),$$

where  $c_0$  and  $c_\tau$  are the initial and current concentrations of vinyl ether **I**, and  $\tau$  is the time.

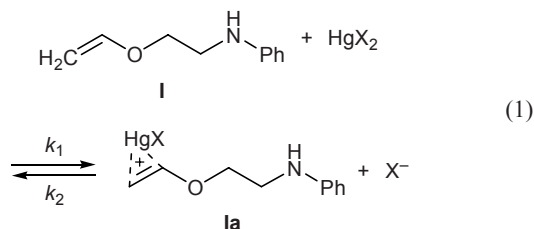
The order of the reaction with respect to the catalyst was determined from the slope of the linear dependences  $\log k_{\text{exp}} - \log c_{\text{cat}}$ , where  $\log k_{\text{exp}} = -0.388 + 1.40 \log c_{\text{Hg(OAc)}_2}$ ,  $r = 0.999$ ,  $s_0 = 0.021$ ;  $\log k_{\text{exp}} = -0.704 + 1.35 \log c_{\text{HgCl}_2}$ ,  $r = 0.999$ ,  $s_0 = 0.008$ .

The non-integer order in the catalyst [1.4 for Hg(OAc)<sub>2</sub> and 1.35 for HgCl<sub>2</sub>] indicates that the catalyst is involved in several steps of the overall multistep process. Let us consider a kinetic scheme which could rationalize the observed non-integer order of the reaction with respect to the catalyst.

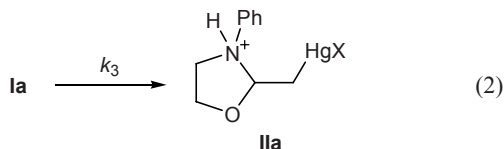
Dependence of the rate constant  $k_{\text{exp}}$  for the isomerization of 2-vinyloxy-*N*-phenylethanamine (**I**) in 1-methylpyrrolidin-2-one, catalyzed by mercury(II) salts  $\text{HgX}_2$ , on the catalyst concentration  $c_{\text{HgX}_2}$  and temperature

$c_{\text{HgX}_2} \times 10^3, \text{M}$	Temperature, °C	$k_{\text{exp}} \times 10^5, \text{s}^{-1}$	$c_{\text{HgX}_2} \times 10^3, \text{M}$	Temperature, °C	$k_{\text{exp}} \times 10^5, \text{s}^{-1}$
Hg(OAc) <sub>2</sub>			Hg(OAc) <sub>2</sub>		
9.36	40	59.66±1.05	1.22	40	3.21±0.05
7.80	40	48.73±0.43	0.69	40	1.70±0.02
6.90	40	40.75±0.61	2.55	45	12.05±0.14
6.24	40	34.51±0.25	2.55	50	15.73±0.19
4.68	40	22.32±0.37	2.55	60	28.10±0.26
4.01	40	18.00±0.21	2.55	70	44.75±0.65
3.83	40	16.93±0.18	HgCl <sub>2</sub>		
3.58	40	14.33±0.11	9.36	40	33.78±0.45
3.12	40	12.61±0.19	3.14	40	7.66±0.09
2.55	40	9.43±0.06	2.51	40	5.50±0.01
1.87	40	6.43±0.07	1.68	40	3.27±0.05

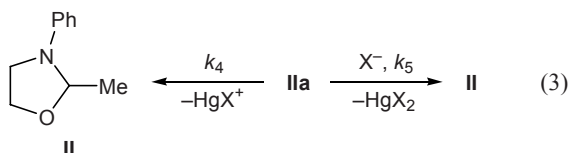
Presumably, the first step is reaction of undissociated catalyst molecule with the substrate, which is similar to that proposed for the first step in the hydrolysis of vinyl ethers in the presence of mercury(II) salts [9].



The second step is intramolecular cyclization of complex **Ia** to give mercurated oxazolidine **IIa**.



In the final step, demercuration of compound **IIa** to oxazolidine **II** can occur both spontaneously and via reaction with  $\text{X}^-$  ion.



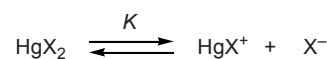
Application of the stationary concentration principle gives the following equations:

$$\begin{aligned}
 k_1 c_{\text{I}} c_{\text{HgX}_2} - k_2 c_{\text{Ia}} c_{\text{X}^-} - k_3 c_{\text{Ia}} &= 0; \\
 c_{\text{Ia}} &= k_1 c_{\text{I}} c_{\text{HgX}_2} / (k_3 + k_2 c_{\text{X}^-}).
 \end{aligned}$$

At low catalyst concentration, i.e., when  $k_3 \gg k_2 c_{\text{X}^-}$ , Eq. (4) is valid:

$$c_{\text{Ia}} = k_1 c_{\text{I}} c_{\text{HgX}_2} k_3^{-1}. \quad (4)$$

The concentration of  $\text{X}^-$  anions is determined by equilibrium (5):



Therefore,

$$c_{\text{X}^-} = (K c_{\text{HgX}_2})^{0.5}. \quad (6)$$

The reaction rate calculated from the gain in the concentration of oxazolidine **II** is given by Eq. (7):

$$\begin{aligned}
 \partial c_{\text{II}} / \partial \tau &= k_4 c_{\text{Ia}} + k_5 c_{\text{Ia}} c_{\text{X}^-} = k_1 k_4 k_3^{-1} c_{\text{I}} c_{\text{HgX}_2} \\
 &+ k_1 k_5 k_3^{-1} c_{\text{I}} c_{\text{HgX}_2} c_{\text{X}^-}.
 \end{aligned} \quad (7)$$

By introducing  $k' = k_1 k_4 / k_3$  and  $k'' = K^{0.5} k_1 k_5 / k_3$  we obtain Eq. (8):

$$\partial c_{\text{II}} / \partial \tau = (k' + k'' c_{\text{HgX}_2}^{0.5}) c_{\text{HgX}_2} c_{\text{I}}. \quad (8)$$

At low catalyst concentrations ( $k' \gg k'' c_{\text{HgX}_2}^{0.5}$ ), Eq. (8) is converted into first-order equation with respect to the substrate and catalyst, while at high catalyst concentrations ( $k' \ll k'' c_{\text{HgX}_2}^{0.5}$ ), the kinetic equation is of first order in the substrate and of an order of 1.5 in the catalyst:

$$\partial c_{\text{II}}/\partial \tau = k' c_{\text{HgX}_2} c_1; \partial c_{\text{II}}/\partial \tau = k'' c_{\text{HgX}_2}^{1.5} c_1.$$

In all intermediate cases, taking into account the first order of the reaction with respect to the substrate, a linear relation should be observed between the experimental rate constant reduced to the catalyst concentration and  $c_{\text{HgX}_2}$ :

$$k_{\text{exp}}/c_{\text{HgX}_2} = k' + k'' c_{\text{HgX}_2}^{0.5} \quad (9)$$

In fact, the experimental rate constants determined at 40°C for different catalyst concentrations (see table) give excellent correlations:

$$\begin{aligned} \text{for Hg(OAc)}_2: k_{\text{exp}}/c_{\text{HgX}_2} &= 0.0062 + 0.615 c_{\text{HgX}_2}^{0.5}; \\ r &= 0.999, s_0 = 0.03; \end{aligned} \quad (10)$$

$$\begin{aligned} \text{for HgCl}_2: k_{\text{exp}}/c_{\text{HgX}_2} &= 0.0062 + 0.32 c_{\text{HgX}_2}^{0.5}; \\ r &= 0.989, s_0 = 0.05. \end{aligned} \quad (11)$$

The existence of correlations (10) and (11) confirms the proposed mechanism for the isomerization of aminoethyl vinyl ethers into oxazolidines.

Insofar as the rate of isomerization is directly proportional to the rate of the first step [ $k_1$ , Eq. (7)], it should depend on the relative stability of intermediate cation **Ia**. Mercury(II) chloride is a much stronger electron acceptor than mercury(II) acetate; therefore, cation **Ia** with X = Cl should be more stable, and  $k_1$  and correspondingly  $k_{\text{exp}}$  should be larger. This is observed experimentally: at equal or similar catalyst concentrations, the reactions catalyzed by  $\text{Hg(OAc)}_2$  are faster by a factor of  $\sim 1.7$  than those catalyzed by  $\text{HgCl}_2$  (see table).

The temperature dependence of the isomerization rate constant of vinyl ether **I** in the presence of mercury(II) acetate fits the Arrhenius equation. The activation parameters calculated for the temperature range 40–70°C (see table) are  $\Delta H^\ddagger = 10.7$  kcal/mol and  $\Delta S^\ddagger = -42.9$  e.u. The high negative entropy of activation indicates that the rate-determining step is intramolecular cyclization ( $k_3$ ) since the other steps either do not involve appreciable change in the number of degrees of freedom ( $k_1$ ,  $k_5$ ) or are accompanied by increase in the number of species ( $k_4$ ), which should

lead to positive entropy of activation. The low enthalpy of activation is consistent with the above conclusion, for the step characterized by the rate constant  $k_3$  almost does not affect the order of binding of atoms.

Thus the results of our kinetic study showed that the cyclization of vinyl ethers derived from amino alcohols into oxazolidines, catalyzed by mercury(II) salts, is a multistep process. The first step is coordination of the mercury atom at the double C=C bond, and next follow intramolecular cyclization (rate-determining step) and demercuration; the latter reaction occurs both spontaneously and by the action of mercury salt anion.

## EXPERIMENTAL

Freshly distilled commercial 1-methylpyrrolidin-2-one and 2-vinyloxy-*N*-phenylethanamine synthesized according to the procedure described in [4] (with a purity of no less than 99.3%, according to the TLC data) were used in kinetic experiments. The purity of the initial compounds was checked, and their identification in the reaction mixture was performed, by gas-liquid chromatography on an LKhM-80 chromatograph equipped with a thermal conductivity detector; carrier gas helium; steel column, 3000×3 mm, packed with 3% of OV-17 on Inerton Super (0.160–0.200 mm); oven temperature programming from 150 to 200°C at a rate of 4 deg/min.

**Isomerization of 2-vinyloxy-*N*-phenylethanamine (I) (kinetic measurements).** Samples of a 2.34 M solution of vinyl ether **I** and of a 0.0936 to 0.0069 M solution of mercury(II) acetate or chloride in 1-methylpyrrolidin-2-one, 5 ml in volume, were adjusted to 40°C and mixed. Samples of the reaction mixture, 1  $\mu\text{l}$ , were withdrawn at definite time intervals using a microsyringe and analyzed by GLC. The concentration of ether **I** was determined by the absolute calibration technique. The chromatographic peak areas were calculated using an I-02 automatic digital integrator.

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