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STUDY ON THE KINETICS OF THE REACTION BETWEEN DIETHYL ESTER OF 1-AMINO-METHYL-ETHANEPHOSPHONIC ACID AND PHENYL ISOCYANATE

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The kinetics of the reaction between O,O-diethyl ester of 1-amino-1-methyl-ethane phosphonic acid and phenylisocyanate, producing diethyl ester of 1-methyl-1-(N-phenylcarbamoyl-amino)ethane phosphonic acid is studied by IR spectroscopy. It is established that the reaction is of second order. The probable scheme of the reaction mechanism is suggested. The rate constant *k* of the initial stage of the reaction is determined. It is established that the rate constant is increased at the advanced stage of the process. The observed enhancement is ascribed to the autocatalytic effect of the reaction product.

Keywords: O,O-diethyl ester of 1-amino-1-methyl-ethanephosphonic acid; phenylisocyanate; kinetic; reaction mechanism

A recent paper[1] reported on the interaction between O,O-diethyl esters of 1-amino-1-methyl-alkanephosphonic acids and different isocyanates or isothiocyanates, producing diethyl esters of 1-methyl-1-(N-substituted carbamoyl- and thiocarbamoyl-amino)-alkanephosphonic acids with high yields. The synthesized compounds showed physiological activity.

It is of interest to study the kinetics of this interaction. No information on the kinetics of similar reactions is available.

The interaction between amines and isocyanates has been studied more thoroughly[2–8] but there still exists no general view about the exact mechanism of the reaction. On the other hand a complete analogy in behavior of the amines and aminophosphonates in their interaction with isocyanates is hardly possible to be derived. With a view to elucidate the mechanism of the title reaction we studied the kinetics of interaction between the diethyl ester of 1-amino-1-methyl-

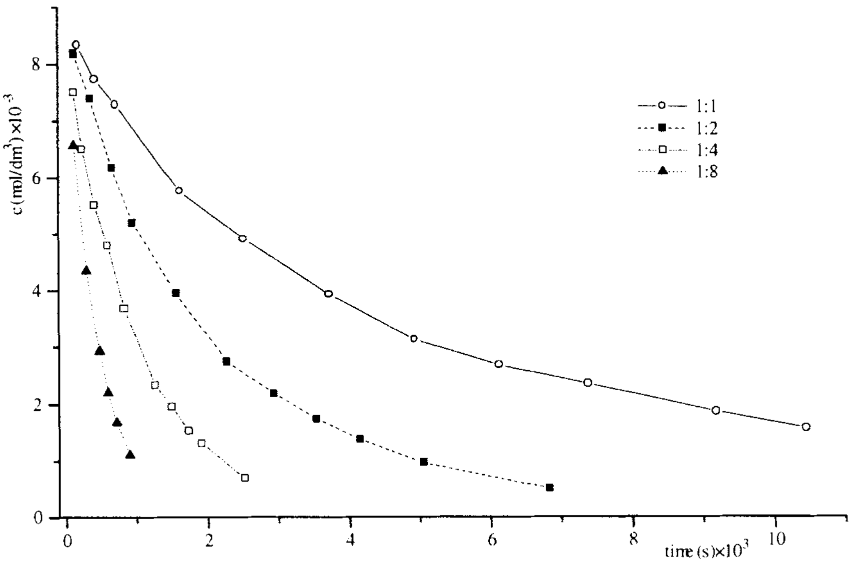


FIGURE 1 Change in concentration of **1** as a function of time. The **1** to **2** molar ratio was varied from 1:1, 1:2, 1:4 to 1:8 at 23°C

ethanephosphonic acid and phenylisocyanate in chloroform medium by IR spectroscopy. The rate of the reaction was checked by the change in molar concentration of the phenyl isocyanate. The latter was evaluated by measuring the intensity of the characteristic band of stretching vibrations of the isocyanate group (-N=C=O) at 2245 cm^{-1}. No bands were recorded in the near spectral range that could complicate the observed spectrum. The change in concentration of the PhNCO as a function of time was followed with varying phenylisocyanate (**1**) to O,O-diethyl ester of 1-amino-1-methyl ethanephosphonic acid (**2**) molar ratio of 1:1, 1:2, 1:4 and 1:8, respectively.

With an initial concentration (c_0) of **1** of 0.85×10^{-2} mol.dm^{-3} the intensity of the -NCO band at 2245 cm^{-1} rapidly decreases with the increase in concentration of **2**. At that the higher the excess the **2** the sharper is the decrease. We suggest that the reaction is of the second order and can be expressed by eq. 1 in the case of diverse initial concentrations of the reagents:

$$-\frac{dc_1}{dt} = k(c_1^0 - c_1)(c_2^0 - c_2) \qquad (1)$$

where c_1^0 and c_2^0 are the initial concentrations of **1** and **2** respectively, while c_1 and c_2 are their current concentrations.

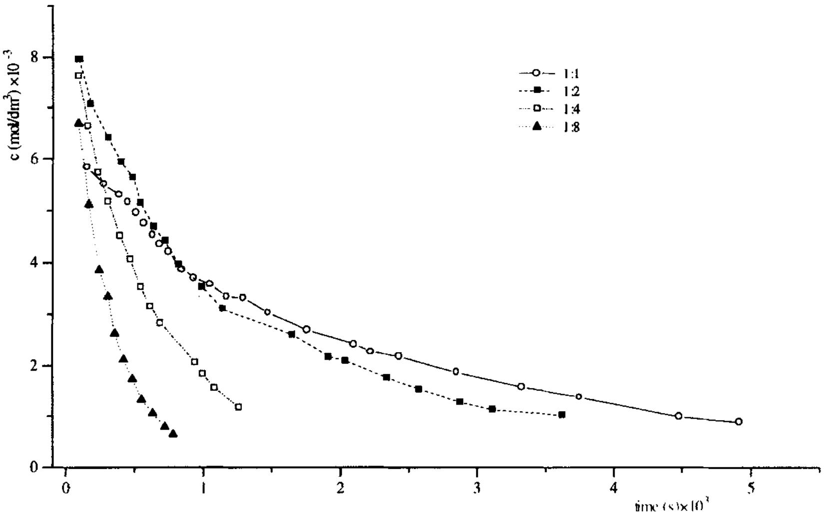


FIGURE 2 Change in concentration of **1** as a function of time. The **1** to **2** molar ratio was varied from 1:1, 1:2, 1:4 to 1:8 at 29°C

In the case of equal concentrations of the reagents the corresponding equation is:

$$-\frac{dc_1}{dt} = k(c_1^0 - c_1)^2 \qquad (2)$$

Expressing c_2 through c_1 and integrating eqs. (1) and (2) one obtains equations (3) and (4).

$$\ln\frac{(c_2^0 - c_1^0) + c_1}{c_1} = k(c_2^0 - c_1^0)t + \ln\frac{c_2^0}{c_1^0} \qquad (3)$$

$$\frac{c_2^0 - c_1^0}{c_1^0 c_1} = kt \qquad (4)$$

Now eqs. (3) and (4) are transformed into eqs. (5) and (6) respectively, by introducing the function Y which is further plotted and discussed in the text.

$$\frac{1}{c_2^0 - c_1^0} \ln(c_2^0 - c_1^0) + c_1 c_1 c_1^0 c_2^0 = kt = Y \qquad (5)$$

$$\frac{c_2^0 - c_1^0}{c_1^0 c_1} = kt = Y \qquad (6)$$

Eq. (5) applies to the reaction with mole ratios of the reagents of 1:2, 1:4 and 1:8. It agrees very well with experimental data as seen in Figures 3, 4.

The curves *a–f* in Figure 3 and 4 illustrate the Y vs. time dependences plotted based on experimental data treated by regression analysis. Curves *a–c* in Figure 3 refer to kinetic studies carried out at 23°, while curves *d–f* in Figure 4—to 29°C, respectively. The mean values of rate constants k are 3.64×10^{-2} $mol^{-1}s^{-1}$ and 5.53×10^{-2} $mol^{-1}s^{-1}$ at 23°C and 29°C respectively. Based on the obtained values for k the activation energy of the reaction was calculated to be $E_a = 47.6$ kJ mol^{-1}.

Having in mind the structure of **2** one could admit that the formation of intermolecular as well as intramolecular H bonds is possible. IR spectral measurements of solutions of **2** in chloroform with concentration ranging from 0.85×10^{-3} $mol.dm^{-3}$ to 0.85×10^{-2} $mol.dm^{-3}$ revealed the absence of a free-NH_2 group. An evidence to this is the fact that the position of the absorption maximum and the profile of the wide band in the range 3200–3500 cm^{-1} characteristic of the N-H stretching vibrations in the -NH_2 group do not change on dilution of the solution (see Figure 5).

The absence of two separate bands at 3350 cm^{-1} for symmetric and at 3450 cm^{-1} for asymmetric N-H vibrations in a free amine group shows that a free-NH_2 group is absent in the molecule of **2**. Hence the formation of an intramolecular bond is more likely to occur and **2** could probably take part in the reaction as a monomer according to the scheme:

An additional indication to the proposed scheme is the appearance of bands of low intensity at 2400 cm^{-1}. They are probably obertones of the P=O band at 1120 cm^{-1}. The formation of intramolecular hydrogen bonds in **2** contributes to the additional polarization of the N-H bond thus facilitating the proton transfer to the nitrogen atom in isocyanate providing that two molecules are too close.

With a mole ratio of **1** to **2** of 1:1 the rate constant is changed in the course of the reaction as seen from Figure 6 and Figure 7.

Values of the rate constants k for the initial stage of the reaction with 1:1 mole ratio of the reagents at 23°C and 29°C, are $4.27.10^{-2}$ and $1.31.10^{-1}$

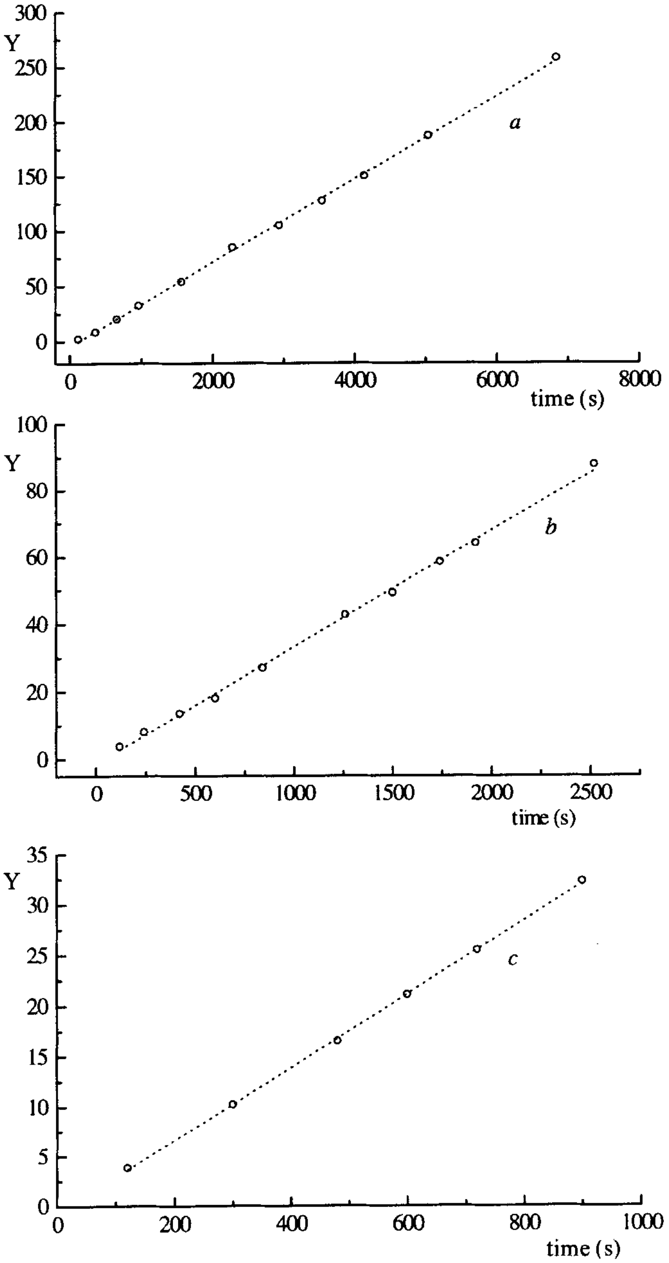


FIGURE 3 Y vs. time dependences at 23°; **1** to **2** molar ratio of 1:2 (*a*), 1:4 (*b*) and of 1:8 (*c*)

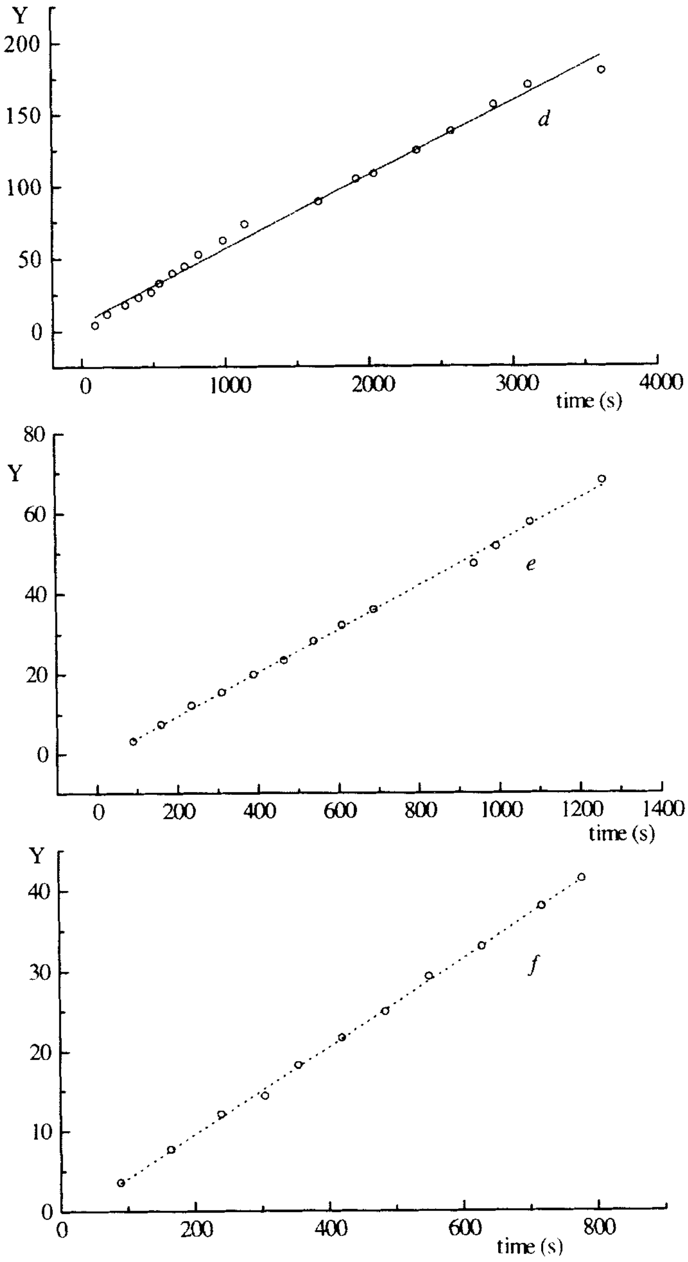


FIGURE 4 Y vs. time dependences at 29°; **1** to **2** molar ratio of 1:2 (*d*), 1:4 (*e*) and of 1:8 (*f*)

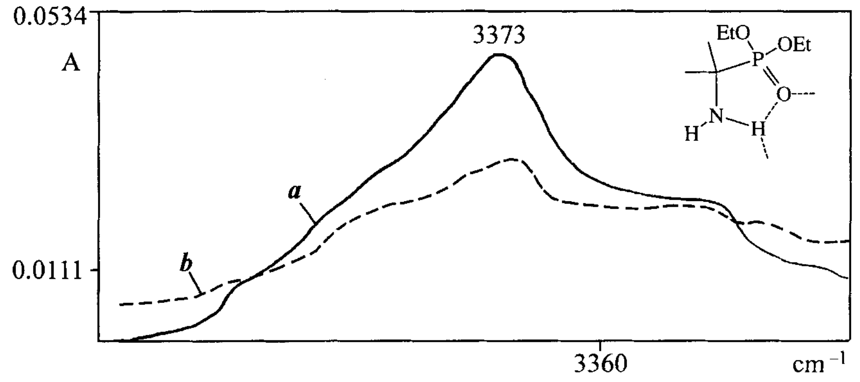
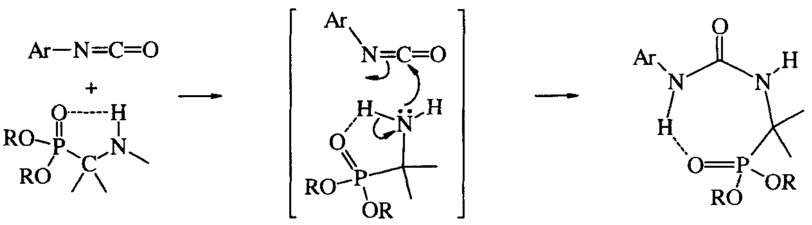


FIGURE 5 IR spectra of solutions of **2** in $CHCl_3$ in 5 cm quartz cuvette (C_a = 0.85 × 10^{-2} mol.dm^{-3} and C_b = 0.85 × 10^{-3} mol.dm^{-3})

mol^{-1}s^{-1} respectively. The enhanced rate constant in the advanced stage of the reaction can be attributed to a weak autocatalytic effect produced by the product O,O-diethyl-1-methyl-1-N-phenyl-carbamoyl amino-ethanephosphonate **3**. This effect is due to the participation of **3** in the electron transfer from **2** to the isocyanate moiety of **1**. Thus the formation of a transient state is realized comprising in the cleavage of the π-bond in N = C and formation of a N-H bond. A similar considerable autocatalyc effect of urea derivatives has been established by other authors[2,4] in reactions between amines and isocyanates. In our case the observed autocatalytic effect is lower judging from the increase in the rate constant value.

In order to obtain additional evidence about the autocatalytic effect of the abovementioned product **3** we carried out the reaction in the presence of **3** with a **1**:**2**:**3** mole ratio of 1:1:1 at 23°C. The calculated rate constant was 5.45 × 10^{-2} mol^{-1}.s^{-1} with a correlation coefficient of 0.997 and standard error of 2.56 × 10^{-3}. The obtained value is commensurable with the value of k'' corresponding to the advanced reaction with a 1:1 mole ratio when product **3** has already been accumulated.



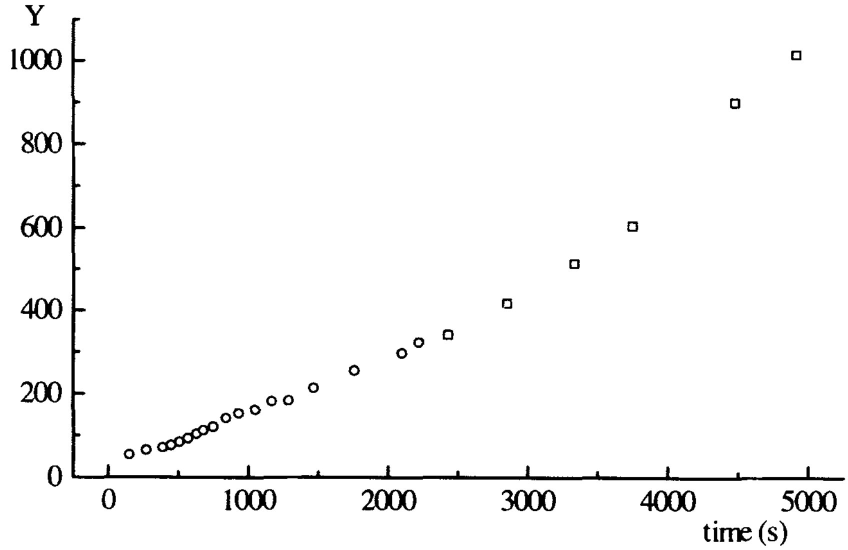


FIGURE 6 Y vs. time dependence at 23° (**1** to **2** molar ratio of 1:1)

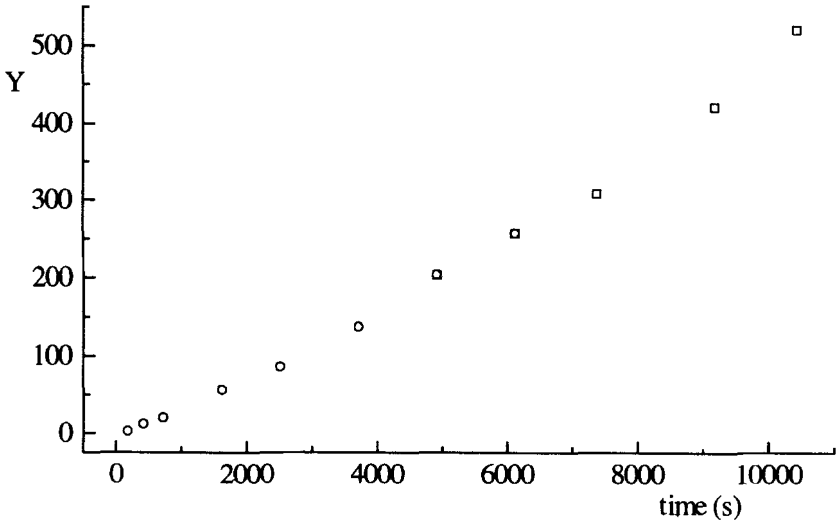


FIGURE 7 Y vs. time dependence at 29° (**1** to **2** molar ratio of 1:1)

EXPERIMENTAL

O,O-diethyl ester of 1-amino-1-methyl-ethanephosphonic acid was synthesized as described elsewhere.[1] Phenylisocyanate was purchased from Merck and was distilled additionall prior to use. Chloroform (Merck) was dried over anhydrous $CaCl_2$ and distilled before use.

SPECORD 75-IR (Carl-Zeiss) and Bomem FT-IR spectrophotometers were used in the experiments.

The experimental data were treated using a regression analysis.

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