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Organic Solvents as Catalysts of Formation of Phosphorus-Containing Thiosemicarbazides

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Abstract—The kinetics of the reaction of *O,O*-diphenyl phosphorohydrazidothioate with phenyl isothiocyanate at 25°C in benzene in the presence of organic bases is studied. The dependences of the catalytic activity on the nature and structure of organic bases and on various parameters characterizing their basicity are analyzed. The catalytic activity exhibited in the formation of phosphorus-containing thiosemicarbazides by donor solvents added to benzene correlates well with both spectroscopic and thermodynamic parameters of basicity: Taft (pK_{HB}), Koppel–Palm (*B*), and Gutmann (*DN*) parameters. A common mechanism of the base catalysis of the thiosemicarbazide formation by organic bases of different classes is suggested and discussed.

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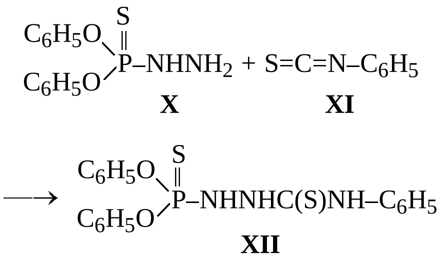
The driving force of the base catalysis in reactions of hydrazine derivatives with isocyanates is donor–acceptor interaction of a nucleophilic agent with a catalyst [1]. Organic solvents can significantly affect this process by interacting with the reaction participants [2].

Therefore, we studied the kinetics of the reaction of *O*,*O*-diphenyl phosphorohydrazidothioate with phenyl isothiocyanate in a benzene solution in the presence of various organic solvents at 25°C. As solvents we chose nitrobenzene **I**, benzonitrile **II**, acetonitrile **III**, ethyl acetate **IV**, diethyl ether **V**, tetrahydrofuran **VI**, dimethylformamide **VII**, tributyl phosphate **VIII**, and dimethyl sulfoxide **IX**. We chose donor solvents containing different base centers and belonging to different classes of organic compounds, capable of specific interaction with the reactants. We proceeded from the assumption that the specific solvation and catalysis are similar in the mechanism. It was important to elucidate the possibility of realization of this mechanism in the reaction system under consideration and to evaluate the catalytic properties of the bases in relation to their nature and structure.

The reaction of *O,O*-diphenyl phosphorohydrazidothioate **X** with phenyl isothiocyanate **XI** in the presence of the above catalysts is irreversible and yields phosphorus-containing thiosemicarbazide **XII**.

We found that the reaction is quantitative, with no side processes. At the same time, small additions of organic bases appreciably accelerate the reaction (Table 1).



$$\underset{\mathbf{X}}{(C_6H_5O)_2P(S)\text{–}NHNH_2} + \underset{\mathbf{XI}}{S{=}C{=}N\text{–}C_6H_5} \longrightarrow \underset{\mathbf{XII}}{(C_6H_5O)_2P(S)\text{–}NHNHC(S)NH\text{–}C_6H_5}$$

The reaction rate in a benzene solution in the presence of organic solvents as catalysts is desribed by Eq. (1):

$$dx/dt = k_0(a - x)(b - x) + k_b(a - x)(b - x)m, \quad (1)$$

where k_0 and k_b are the rate constants of the noncatalytic ($l\,mol^{-1}\,s^{-1}$) and catalytic ($l^2\,mol^{-2}\,s^{-1}$) reactions, respectively; *a*, *b*, and *m*, initial concentrations of hydrazide, phenyl isothiocyanate, and catalyst, respectively (M); *x*, product yield (M); and *t*, time (s). It follows from Eq. (1) that the apparent rate constant of the overall process is determined from Eq. (2):

$$k = k_0 + k_b m. \quad (2)$$

For the catalyzed reaction, the apparent rate constants (k, $l\,mol^{-1}\,s^{-1}$) were found from the second-order rate equation, because the reciprocal running concentration at various concentrations of catalysts was a linear function of time and the rate constants did not change during the process. A linear relationship was observed between the apparent rate constant *k* and catalyst concentration (up to ~0.05 M). The

Table 1. Apparent (k) and catalytic (k_b) rate constants of the reaction of *O,O*-diphenyl phosphorohydrazidothioate with phenyl isothiocyanate at various concentrations of solvents-catalysts in benzene at 25°C ($a = b = 0.00125$ M)

Solvent	Solvent concentration, M	$k \times 10^3$, l mol^{-1} s^{-1}	k_b, l^2 mol^{-2} s^{-1}
I	0.01	1.08 ± 0.02	0.0984
	0.02	1.95 ± 0.06	0.0927
	0.03	2.90 ± 0.09	0.0939
II	0.001	0.343 ± 0.042	0.247
	0.005	1.30 ± 0.07	0.241
	0.01	2.55 ± 0.08	0.245
III	0.001	0.436 ± 0.025	0.340
	0.0025	0.966 ± 0.038	0.348
	0.005	1.82 ± 0.05	0.346
IV	0.005	2.11 ± 0.07	0.402
	0.01	4.15 ± 0.31	0.405
	0.05	20.6 ± 2.3	0.410
V	0.005	2.29 ± 0.09	0.458
	0.0075	3.52 ± 0.26	0.457
	0.01	4.62 ± 0.39	0.452
VI	0.005	3.26 ± 0.24	0.632
	0.0075	4.80 ± 0.30	0.627
	0.01	6.38 ± 0.42	0.628
VII	0.0005	0.635 ± 0.037	1.08
	0.001	1.15 ± 0.05	1.06
	0.002	2.19 ± 0.07	1.04
VIII	0.0005	0.656 ± 0.030	1.12
	0.00075	0.921 ± 0.043	1.10
	0.001	1.21 ± 0.05	1.11
IX	0.0005	0.836 ± 0.037	1.48
	0.00075	1.20 ± 0.05	1.48
	0.001	1.55 ± 0.06	1.45

rate constants of the catalyzed reaction (k_b) given in Tables 1 and 2 were determined from Eq. (2) using data from Table 1 ($k_0 = 0.0958 \times 10^{-3}$ l mol^{-1} s^{-1} [3]). The rate constants of the noncatalytic and catalytic reactions calculated graphically and from Eq. (2) are in good agreement.

Tables 1 and 2 show that bases belonging to different classes strongly differ in the activity. The catalytic activity of the solvents, evaluated as the ratio k_b/k_0, is within 992–15344 (Table 2), i.e., the least and the most active catalysts differ in the activity by a factor of more than 15. The most active catalyst is dimethyl sulfoxide **IX**; its nucleophilic solvating power is the highest. The catalytic activity of the examined solvents varies in parallel with their capability for specific solvation. The most catalytically active solvents are dimethyl sulfoxide, tributyl phosphate, and dimethylformamide; their catalytic activity ranges from 11064 to 15344. Nitrobenzene, nitriles, ethers, and esters are less active; their catalytic activity ranges from 992 to 6566. The catalytic activity of solvents increases in the following order: aromatic nitro compounds < nitriles < carboxylic acid esters ≈ ethers < carboxylic acid amides ≈ phosphoric acid esters < sulfoxides. Thus, the catalytic activity correlates with the capability of the compounds to act as electron donors in the interaction with proton donors, which increases in the same order.

To elucidate the mechanism of the catalytic effect of various electron-donor solvents, it was appropriate to construct a quantitative relationship between the catalytic activity of the catalysts and parameters characterizing their properties. An attempt to construct a correlation between the logarithms of the catalytic rate constants k_b and the basicity of the solvents in water (pK_{BH^+}) failed (Table 2). Therefore, we can conclude tha the reaction does not involve complete dissociation into ions with the proton transfer from the hydrazide to the catalyst. At the same time, the catalytic activity of the solvents varies in the same direction as

Table 2. Influence of the characteristics of organic solvents on the rate of the reaction of *O,O*-diphenyl phosphorohydrazidothioate with phenyl isothiocyanate in benzene at 25°C

Solvent	pK_{BH^+} [4]	pK_{HB} [4]	*DN* [5, 6]	*B* [6, 7]	k_b, l^2 mol^{-2} s^{-1}	k_b/k_0, l mol^{-1}
I	–12.14	0.73	4.4	67	0.0950 ± 0.0074	992
II	–10.70	0.80	11.9	155	0.244 ± 0.008	2547
III	–	0.90	14.1	160	0.345 ± 0.010	3601
IV	–3.96	1.09	17.1	181	0.406 ± 0.010	4238
V	–2.42	1.01	19.2	280	0.456 ± 0.008	4760
VI	–2.08	1.26	20.0	287	0.629 ± 0.006	6566
VII	–1.50	2.06	26.6	291	1.06 ± 0.05	11064
VIII	–	2.24	23.7	336	1.11 ± 0.02	11587
IX	–1.04	2.53	29.8	362	1.47 ± 0.04	15344

their capability for hydrogen bonding, described by the quantity pK_{HB} [2, 4, 8, 9]. The catalytic effect of donor solvents on the rate of the reaction of *O,O*-diphenyl phosphorohydrazidothioate with phenyl isothiocyanate is described by the following correlation of k_b with pK_{HB}:

$$\log k_b = (-1.02 \pm 0.11) + (0.507 \pm 0.080)\mathrm{p}K_{HB}, \quad (3)$$
$$n\ 9,\ r\ 0.933,\ s\ 0.142.$$

The existence of this correlation indicates that the catalytic effect of solvents is due to only partial withdrawal of a proton from the hydrazide via hydrogen bonding. Therefore, it can be suggested that catalysts of diverse nature act by the same mechanism, presumably by the mechanism of general base catalysis, involving formation of an H bond (structure **XIII**). The fact that correlation (3) covers both weak and strong bases also counts in favor of the suggested mechanism. It should be noted that isocyanate molecules have very weakly pronounced coordination properties and do not form complexes even with very strong electron donors [10–12].

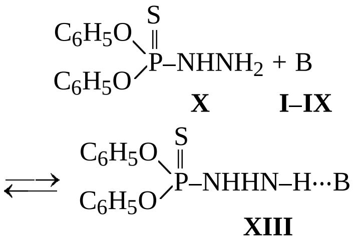
An important quantitative parameter of donor solvents is their donor number [5, 13]. The donor number characterizes the overall intensity of the interaction of an electron donor with an acceptor molecule. As seen from Table 2, the catalytic activity of the solvents increases with an increase in their donor number. This trend is quantitatively described by linear relationship (4):

$$\log k_b = (-1.18 \pm 0.06) + (0.0470 \pm 0.0029)DN, \quad (4)$$
$$n\ 9,\ r\ 0.987,\ s\ 0.064.$$

The nucleophilic solvating power of solvents is quantitatively characterized by their Koppel–Palm basicity (parameter *B*) [7, 14]. As expected, this quantity also lienarly correlates with the logarithms of the catalytic rate constants:

$$\log k_b = (-1.16 \pm 0.11) + (0.00361 \pm 0.00043)B, \quad (5)$$
$$n\ 9,\ r\ 0.954,\ s\ 0.120.$$

These facts allow us to consider the catalysis mechanism as preassociative (a particular case of general base catalysis) and common for all the examined solvents belonging to different classes of organic compounds. The first step [scheme (6)] involves association of hydrazide **X** with a solvent molecule B (B is **I**–**IX**) with the formation of hydrogen-bonded complex **XIII**. The association is a fast and reversible process.

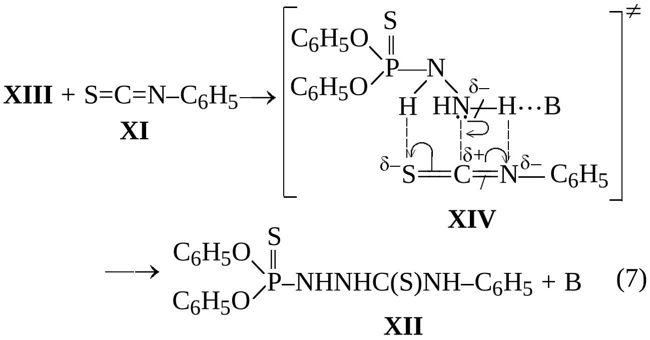


X **I**–**IX**

XIII

(6)

The second step [scheme (7)] is rate-determining and involves the reaction of associate **XIII** with phenyl isothiocyanate **XI**. The increased nucleophilicity of the hydrazide in the associate facilitates formation of a new bond with the carbon atom of the isothiocyanate in the cyclic transition state **XIV**; this is followed by the transformation into the reaction product, thiosemicarbazide derivative **XII**, with the regeneration of the catalyst **I**–**IX**.



XI

XIV

XII

(7)

Thus, the formation of phosphorus-containing thiosemicarbazides in a benzene solution, catalyzed by electron-donor solvents, follows a common mechanism of general base catalysis involving fast equilibrium formation of a hydrogen-bonded (N–H···B) prereaction complex followed by its reaction with the substrate.

EXPERIMENTAL

Benzene was purified as described in [15]. Nitrobenzene (analytically pure grade) was dried over calcium chloride and distilled twice in a vacuum. Benzonitrile (chemically pure grade) was refluxed for 5 h over phosphorus pentoxide and then distilled twice without the desiccant at a reduced pressure. Acetonitrile (analytically pure grade) was refluxed for 3 h over phosphorus pentoxide and then distilled two times from fresh portions of P_2O_5 and the third time without the desiccant. Ethyl acetate (pure grade) was washed with a saturated aqueous solution of NaCl, dried for a week over magnesium sulfate, and then distilled two times from fresh portions of P_2O_5 and the third time without the desiccant. Diethyl ether and tetrahydrofuran (pure grade) were refluxed over KOH and distilled on a column from sodium. Dimethylformamide (pure grade) was kept for 3–4 h under reduced pressure of nitrogen to remove low-boiling amines, the low-boiling fraction was distilled off, and the residue was refluxed for 2 h with hexamethylene diisocyanate (10 ml l^{-1}) and distilled three times on a column, with the collection of the fraction boiling at 55°C (20 mm Hg). Tributyl phosphate (pure grade) was vacuum-distilled. Dimethyl sulfoxide (pure grade) was distilled at a reduced pressure from barium oxide and then two times without the desiccant; the first and the last fractions were discarded. *O,O*-Diphenyl phosphorohydrazidothioate was prepared from the corresponding acid chloride and hydrazine hydrate and was purified as described in [16, 17]. Phenyl isothiocyanate was vacuum-distilled just before use. The physicochemical constants of all the chemicals used agreed with the published data.

The reaction progress in benzene in the presence of organic catalysts was monitored as described previously [18]. The kinetic experiments were performed in benzene at 25 ± 0.05°C. The initial concentration of the reactants was 1.25×10^{-3} M; the catalyst concentration was varied from 0.0005 to 0.05 M.

The accuracy of the results was evaluaed by methods of mathematical statistics [19] at a confidence level of 0.95.

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