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Kinetics and Mechanism of Quaternization of Tertiary Phosphines with Unsaturated Carboxylic Acids. Kinetic Studies of the Reactions in Aprotic Solvents

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Abstract—Data obtained while studying the kinetics of quaternization of tertiary phosphines with the unsaturated carboxylic acids in the series of aprotic solvents indicate the participation of a second molecule of acid playing the part of the external proton donor in this process. Quantitative analysis of the effect of solvent within the frames of the Koppel–Palm equation showed that the main contribution in the reaction rate belongs to the nucleophilicity of medium while the effects of polarity and electrophilicity are smaller. The results obtained suggest the step-by-step mechanism of interaction including the formation of the zwitterionic intermediate on the reaction pathway common for the solvents with different proton activity.

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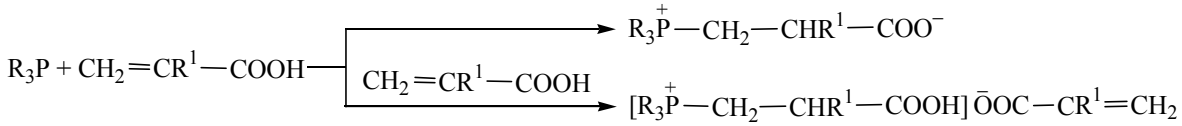
We have reported recently on the results of kinetic studies of the reaction of triphenylphosphine with the unsaturated carboxylic acids in the protic solvents like alcohols and the acetic and propionic acids [1, 2]. The leading feature of this investigation occurred to be the peculiar inertness of carboxylic proton in the composition of the unsaturated carboxylic acid attacked by phosphine. It consists in the absence of migration of this proton in the chosen solvent by means of intramolecular mechanism to the carbanion center appearing in the course of the reaction. As a result the proton transfer proceeds according to intermolecular mechanism from the medium. In the carboxylic acids it takes place from the solvent, while in alcohols it proceeds according to two parallel pathways from the solvent and the second molecule of substrate present in the solvent.

Nevertheless, the problem of principal existence of intramolecular pathway of proton transfer in the process under study remains unsolved, and this article deals with the attempts to establish this fact. For this purpose kinetics of the reaction of triphenylphosphine with acrylic acid was studied in the series of aprotic solvents including acetonitrile, sufolane, diethyl carbonate, ethyl and butyl acetate, DMF, and DMSO. Proton transfer in these solvents is possible only with the participation of the substrate.



R_3P = Ph_3P, Ph_2PMe, $PhPMe_2$; R^1 = H, Me.

This hypothesis was confirmed experimentally. In these solvents a general third order was established including the first order in the triphenylphosphine and the second order in the acid (Fig. 1). It indicates the necessity of participation of the second molecule of acrylic acid as the proton donor in the process of quaternization in aprotic solvents.

Kinetic equation of the reaction has the form (1):

$$W = k'C_p = k_{III}C_pC_a^2. \quad (1)$$

Here C_a is the concentration of acrylic acid, C_p is the concentration of phosphine, k_{III} is the third order rate constant, $k' = k_{III}C_a^2$ is the pseudofirst order rate constant at $C_a >> C_p$.

The validity of kinetic Eq. (1) for the aprotic solvents is confirmed also by an example of methyldiphenyl- and dimethylphenylphosphine and also the other unsaturated carboxylic acid, the methacrylic one. Hence, the use of aprotic solvents permitted proving directly that the quaternization process under study has the general third order. For the alcohols and carboxylic acids capable of playing the role of the proton-donating agent such proof can be only indirect because the order by solvent in contrast to the order by substrate cannot be evaluated directly from the kinetic experiment. The conclusion on the including the concentration of the proton-donating solvent in the kinetic equation of the reaction was made previously on the basis of comparison of the kinetic data for the reactions of triphenylphosphine with the unsaturated carboxylic acids and their esters, of the study of the kinetics of the reaction in the mixtures of acetic acid with the aprotic solvent, acetonitrile, and also because of the existence of the common isokinetic dependence for different channels of proton transfer [1, 2]. For the carboxylic acids (acetic, propionic) kinetic Eq. (2) is valid.

$$W = k_{III,s}C_sC_pC_c. \quad (2)$$

For alcohols it has the form of superposition (3).

$$W = k_{III,s}C_sC_pC_a + k_{III}C_pC_a^2. \quad (3)$$

Here C_s is the concentration of proton-donating solvent, $k_{III,s}$ is the third order rate constant with the participation of the given solvent. Equations (2) and (3) are partial cases of the Eq. (1).

Kinetic and activation parameters of the reactions under study are listed in the table.

In this case the common isokinetic dependence log k_{T+30}–log k_T is observed for the reaction of triphenylphosphine with the acrylic acid in alcohols, carboxylic acids, and the aprotic solvents. It includes also data for the reactions of methyldiphenyl- and dimethylphenylphosphine.

$$\log k_{T+30} = 0.915\log k_T + 0.482, \quad (4)$$
$$N\ 19,\ R\ 0.9995,\ s\ 1.35\times10^{-3}.$$

Isokinetic dependence (4) including 19 points in the range of more than four logarithmic units for the data on the reactions of tertiary phosphines with the acrylic acid in the aprotic solvents, alcohols, and carboxylic acids presented in Fig. 2. It can be complemented by the points for methacrylic acid:

$$\log k_{T+30} = 0.915\log k_T + 0.481,$$
$$N\ 21,\ R\ 0.9995,\ s\ 1.23\times10^{-3}.$$

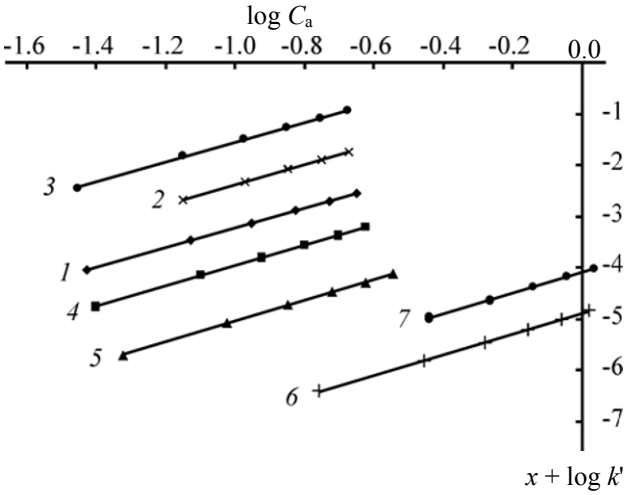


Fig. 1. Evaluation of order with respect to acrylic acid in the reaction with triphenylphosphine in the aprotic colvents: (*1*) MeCN: log k' = 1.92 log C_a – 1.30, R = 1.000; (*2*) sulfolane: 1 + log k' = 1.97log C_a – 0.41, R = 0.9999; (*3*) $(EtO)_2CO$: 2 + log k' = 1.94 log C_a + 0.38, R = 0.9994; (*4*) BuOAc: log k' = 1 97 log C_a – 1,98, R = 0.9999; (*5*) EtOAc: log k' – 1 = 2.02log C_a – 3.03, R = 1.000; (*6*) DMF: log k' – 1 = 2.02log C_a – 4.88, R = 0.9995; (*7*) DMSO: log k' = 2.01 log C_a – 4.09, R = 0.9995.

Analogous isokinetic dependence was obtained previously for the series of the reactions of triphenylphosphine with unsaturated carboxylic acids in the acetic acid medium [1]. It shows that all the reactions studied in this work and in the previous ones belong to one general array where the main features of the reaction mechanism are preserved independent of the nature of phosphine, of the unsaturated carboxylic acid, and of the proton donor in the final act of the reaction.

As seen from the table, the rate of the reaction increases in the series triphenylphosphine–methyldiphenylphosphine–dimethylphenylphosphine with the increase in the nucleophilicity of phosphine and the decrease in sterical hindrances around the phosphorus atom indicating the general nucleophilic character of the reaction. The introduction of a methyl group instead of one of the phenyl substituents increases the reactivity of tertiary phosphine in this process approximately ten-fold. It is known that the quaternization of phosphines with alkyl halides may be described by the one-parametric Taft Eq. (5) [3]:

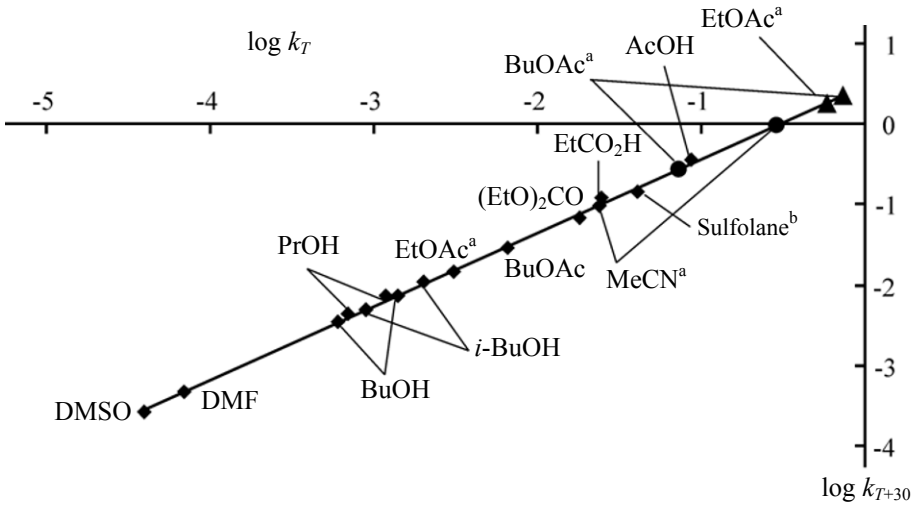


Fig. 2. Common isokinetic dependence log k_{T+30}–log k_T for the reactions of triphenyl- (rhombs), methyldiphenyl- (small circles), and dimethylphenylphosphins (triangles) with the acrylic acid in different solvents (T = 283[a], 293, 303[b] K for sulfolane).

$$\log k = \log k_0 + \rho^* \Sigma\sigma_i^*. \quad (5)$$

Here $\Sigma\sigma_i^*$ is the summary inductive effect of substituents on phosphorus atom. Considering that σ^*_{Me} = 0.00 and σ^*_{Ph} = +0.60 we can find that Eq. (5) is also valid for the quaternization of the triad of phosphines under study with the acrylic acid (Fig. 3):

$$\log k_{III} = -1.76\Sigma\sigma_i^* + 1.16, \quad (6)$$
$$N\ 3,\ R\ 0.998,\ s\ 6.94\times10^{-3}.$$

In Eq. (6) the data for ethyl acetate were used. Analogous equation can be obtained also for butyl acetate:

$$\log k_{III} = -1.82\Sigma\sigma_i^* + 1.34,$$
$$N\ 3,\ R\ 0.998,\ s\ 9.51\times10^{-3}.$$

The difference in reactivity of the acrylic, methacrylic, and other acids we considered previously [1].

Data presented in the table permit the analysis of the effect of solvent on the rate of the reaction between triphenylphosphine and the acrylic acid and an important conclusion on its mechanism. There exists the following grading of solvents by the rate of interaction. The highest rate is observed in the solvents incapable of strong specific solvation of acid like acetonitrile, sulfolane, and esters. In the series of these solvents the rate is higher for polar media like acetonitrile and sulfolane indicating the polarity of the transition state. At the transfer to the less polar esters the reaction rate constant decreases though insignificantly. For the solvents capable of formation of strong hydrogen bond with the molecule of substrate like dimethylformamide and dimethylsulfoxide a sharp decrease in the reaction rate was found, and even the high polarity of these solvents cannot significantly compensate it. The last effect is quite logical because it follows from the kinetic data that the stage of proton transfer influences the general reaction rate and can

Kinetic and activation parameters of the reactions of tertiary phosphines with unsaturated carboxylic acids in the aprotic solvents (30°C)

R_3P	Solvent	n[a]	$k_{III}\times10^3$, $l^2\ mol^{-2}\ s^{-1}$	$\Delta H^{\neq}$, kcal mol^{-1}	$-\Delta S^{\neq}$, e.u.
			Acrylic acid		
Ph_3P	MeCN	1.92	55.9	7.2	40
	Sulfolane	1.97	40.3	7.7	39
	$(EtO)_2CO$	1.94	25.4	7.6	40
	BuOAc	1.97	10.6	8.5	39
	EtOAc	2.02	9.1	8.1	41
	DMF	2.02	0.14	11.4	39
	DMSO	2.01	0.08	10.4	43
Ph_2PMe	MeCN	1.92	569	6.2	39
	BuOAc	1.96	172	7.2	38
	EtOAc	2.00	131	7.0	39
$PhPMe_2$	BuOAc	1.95	1610	6.1	37
	EtOAc	1.91	1170	6.0	38
			Methacrylic acid		
Ph_2PMe	BuOAc	1.96	3.5	9.2	40
$PhPMe_2$	BuOAc	1.91	33.3	7.8	39

[a] n is the experimental reaction order with respect to the unsaturated acid

limit it. This is why the solvent capability of the specific solvation of acid is the determining factor and negatively affects the rate of the process.

But special interest for the establishing the mechanism of the reaction of tertiary phosphines with the unsaturated carboxylic acids presents the quantitative consideration on the effect of solvent, namely the establishment of the correlation of the rate constant k_{III} with some empirical parameter of solvent. The attempts to correlate the values of rate constants with the Kirkwood polarity of solvent Y, the Gutmann acceptor numbers AN, the Mayer donor numbers DN, and the Dimroth–Reichardt parameters E_T and E_T^N within the frames of one-parametric and two-parametric relationships failed. This fact was not unexpected because for the complex multi-step processes where the specific interaction between the solvent and the substrate takes place establishing such correlations is complicated if ever possible.

Generalization of the experimental data became possible with the help of Koppel–Palm equation considering the contribution of all four parameters of solvent, that is, of its polarity Y, polarisability P, characterizing the ability of the solvent to nonspecific solvation, the electrophilicity (total acidity) E, and nucleophilicity (total basicity) B characterizing the ability of the solvent to specific solvation. Note that the Koppel–Palm equation very well describes the effect of the solvent on the analogous process of quaternization of amines with the prevailing contributions of electrophilicity and polarity of the medium [5]. The above-mentioned equation is also applicable to the reaction of quaternization of tributylphosphine with hydrogen sulfide, though with some limitations [6].

Processing of these data with the help of the regression analysis method revealed the good correlation coefficient for the valuable contribution of

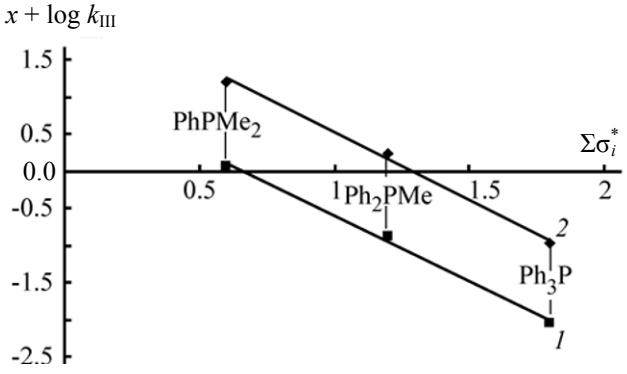


Fig. 3. Dependence of log k_{III} on $\Sigma\sigma_i^*$ for the reaction of tertiary phosphines with the acrylic acid at 30°C in (*1*, x = 0) EtOAc and (*2*, x = 1) BuOAc.

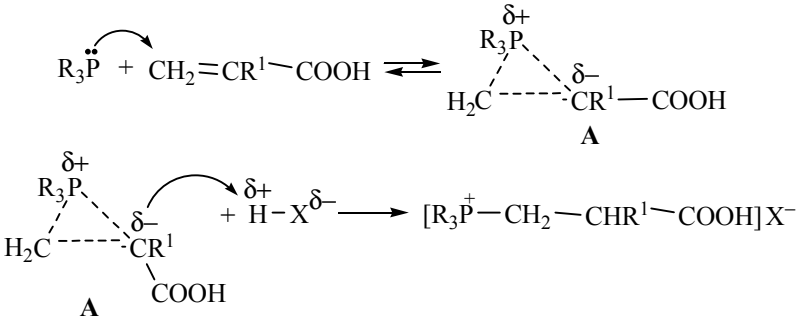
three parameters of solvents, that is, of their polarity and electrophilicity favoring the reaction, and nucleophilicity impeding it:

$$\log k_{III} = (1.26\pm0.31)Y + (7.5\pm0.5)\times10^{-2}E - (1.5\pm0.6)\times10^{-2}B,$$
$$N\ 6,\ R\ 0.981,\ s\ 0.105. \qquad (7)$$

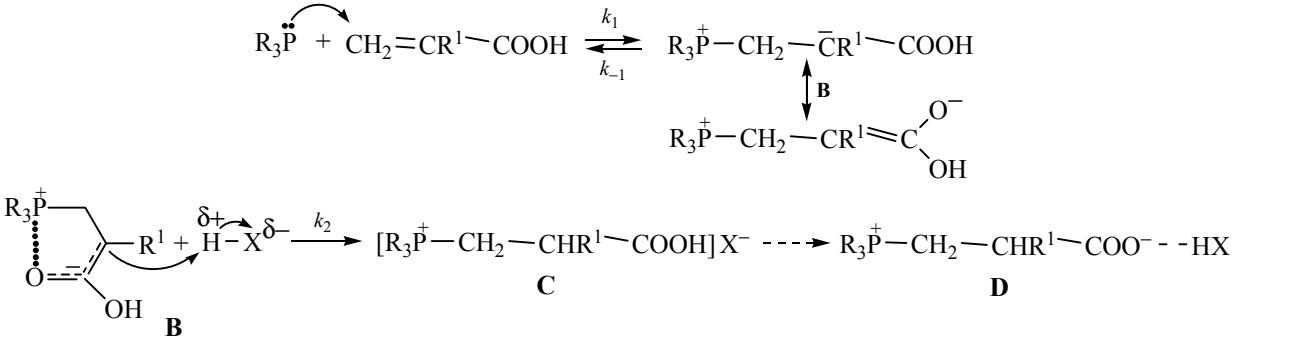
Free member in the correlation Eq. (7) is equal to zero indicating that in the gas phase the rate constant is equal to 1. In the calculations the data related to six solvents were used (see the table). Butyl acetate was excluded because its parameters of specific solvation are not reported.

The studies performed showed that most significant is the contribution of nucleophilicity of the medium hampering the proceeding of the final stage of the reaction, of the proton transfer. Besides, nucleophilic solvation negatively affects the rate of nucleophilic attack of phosphine because the formation of a hydrogen bond decreases the electrophilicity of the terminal carbon atom of the C=C bond. A satisfactory correlation can be obtained using only one B parameter:

$$\log k_{III} = -(1.1\pm0.5)\times10^{-2}B,$$
$$N\ 6,\ R\ 0.969.\ s\ 0.155.$$



HX = R^2COOH, $CH_2=CR^1–COOH$, R^3OH.



Step-by-step mechanism of the reaction of tertiary phosphines with the unsaturated carboxylic acids [1, 2] including the formation of low polar prereactional complex **A** where occurs the formation of the full-value covalent P–C bond simultaneously with the transfer of proton on the forming carbanion center we considered previously as the main version.

But the performed quantitative analysis of the effect of solvent revealing the valuable contribution of the polarity of the medium made us to change our opinion in favor of the mechanism with the polar zwitterion intermediate **B** on the reaction pathway which was at first considered less probable.

In the zwitterions **B** the carbanionic charge is stabilized by the resonance with the adjacent carboxy group causing the decrease in the acidity of proton of this group in the molecule of the unsaturated carboxylic acid attacked by phosphine. As the reaction mixture always contains more acidic proton of another molecule of the carboxylic acid which is not attacked by phosphine or a more available proton of the solvent (in the case of protic solvents) the migration of proton from the carbanion center proceeds according to the intermolecular mechanism from the medium, and the kinetic curve of the reaction always has general third order. As additional factor in the stabilization of intermediate **B** may serve the existence of electrostatic interaction between the phosphonium center and the negative charge on oxygen atom of the conjugated enol. The existence of such non-covalent interaction in the analogous structures is confirmed by quantum-chemical calculations [7] and X-ray studies [8]. The electrophilic solvation also influences the anionic charge of the intermediate **B**.

According to the presented scheme of mechanism the apparent third order reaction rate constant is the empirical value which can be represented as the product of elementary constants of separate reaction steps.

$$k_{III} = k_3k_2 = (k_1k_2)/k_{-1}.$$

This fact needs certain caution in the interpretation of kinetic data, in particular,l of activation parameters which are determined from k_{III} and hence are apparent values. But for such kinetic schemes these drawbacks are minimal because the equilibrium constans are significantly less sensitive to temperature than the rate constants.

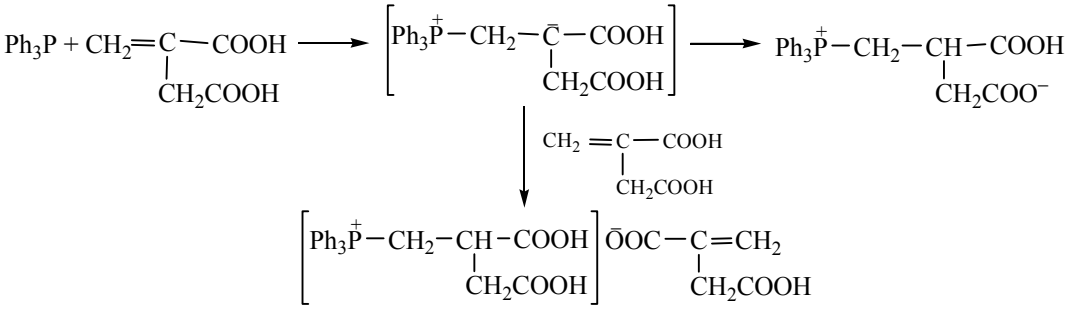
As seen from the table, the use of sterically less hindered phosphines of high nucleophilicity decreases the free activation energy of the reaction. The introduction of methyl substituents instead of the phenyl ones not only increases the rate of the direct reaction k_1 due to the increase in the nucleophilicity of phosphine, but also decreases the rate of the reversed process k_{-1} due to more effective stabilization of the intermediate **B** by the electrostatic interaction of the phosphonium and anionic centers. Joined effect of both factors leads to the noticeable increase in the effective rate constant k_{III}.

A significant contribution in the free activation energy of the process under study brings the entropy component. High negative $\Delta S^{\neq}$ values show the high ordering of the transition state of the reaction. They are characteristic of the processes proceeding with strong charge separation.

While selecting the solvent for performing the reaction of tertiary phosphines with unsaturated carboxylic acids the preference must be given to those incapable of strong specific solvation of the acid. Polarity and electrophilicity of solvent favor the proceeding of the reaction, but the effect of these factors on the reaction rate is less pronounced. The increase in the reaction rate may be achieved by using solvents capable of be involved into the proton transfer (for example, acetic acid and methanol).

Hence, the investigation performed permitted drawing a general picture of quaternization of tertiary phosphines with unsaturated carboxylic acids which is

always described by the third order kinetic equation, but due to the different proton activity of solvent in each definite case its partial versions [(1), (2), or (3)] may take place. This statement does not correspond to unsaturated dicarboxylic acids whose second carboxy group may be involved in the proton transfer according to intramolecular mechanism as for example in the case of itaconic acid [9].



A practical conclusion from this studies is that in fact the primary reaction product is the phosphonium salt **C** and not the carboxylate betaine **D**. Depending on the basicity of both centers compound **C** either does not alter or transforms into the carboxylate betaine **D** stabilized by the proton-donating molecule. These data explain high protophilicity of carboxylate phosphobetaines. At first it was suggested that the role of proton-donating reagents is the stabilization of carboxylate center of the quaternization adduct [10], but *a posteriori* it may be stated that the first reason of their protophilicity is the mechanism of formation because the phosphonium salt always lies on the reaction pathway. The studies performed clearly show how investigation of the reaction mechanism permits to understand the peculiarity of structure and thermodynamic stability of the reaction products.

The data obtained in the course of these studies broaden our notions on the processes of proton migration taking place in the majority of the phosphine-catalyzed reactions [11] and also in many enzyme reactions in living organisms where the role of proton transfer agent is played by the water molecule [12].

EXPERIMENTAL

The study was carried out using the spectrophotometric method on a Perkin Elmer Lambda 35 apparatus according to the procedure described previously [1, 2] at λ 300 nm for triphenylphosphine, at λ 290 nm for methyldiphenylphosphine, and at λ 280 nm for methyldiphenylphosphine. While working with the oxygen-sensitive methyldiphenylphosphine and dimethylphenylphosphine the solvents before use were additionally flown with dry nitrogen to remove dissolved oxygen. Experimental error while evaluating of the rate constants was no more than ±5%.

Starting reagents (triphenylphosphine, acrylic and methacrylic acids) and also solvents were used as the commercial products purified additionally according to the routine procedures [13–16]. Methyldiphenylphosphine (Alfa Aesar, 99%) and dimethylphenylphosphine (Sigma Aldrich, 97%) were kept in the sealed ampules under argon and used without the additional purification.

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