Solvent Effect on Kinetics and Mechanism of the Phospha-Michael Reaction of Tertiary Phosphines with Unsaturated Carboxylic Acids

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ABSTRACT: In aprotic solvents, kinetics of the reaction of triphenylphosphine with acrylic acid is second order in the acid and first order in the phosphine. To find the most suitable model to describe the solvent effect on this reaction, the third-order rate constants in a series of 16 aprotic solvents were analyzed using one- and multiparameter regressions within the framework of the Kamlet-Taft, the Catalán, the Gutmann-Mayer, and the Koppel-Palm equations. The best result gives a two-parameter model constructed on the basis of the Reichardt polarity E_T and the basicity B from the Koppel-Palm equation, with the weak positive effect of the E_T parameter on the reaction rate and very strong negative effect of the B parameter. The results obtained give further evidence to the previously suggested a stepwise mechanism, which involves the initial formation of a zwitterionic intermediate, followed by the proton transfer from the second molecule of acrylic acid to the generated carbanionic center in the rate-determining step. © 2014 Wiley Periodicals, Inc. Heteroatom Chem. 00:1–12, 2014; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21161

INTRODUCTION

The Michael reaction, the conjugate addition of a nucleophile to the α , β -unsaturated carbonyl and related compounds (Scheme 1) is one of the most versatile and powerful tools in organic synthesis [1].

Undiminishing interest of chemists to this reaction can be attributed to its several advantages, viz. (i) the ability to combine different nucleophiles (Michael donors) and activated alkenes (Michael acceptors) with each other, giving a rise to synthetically useful products with novel C-C, C-O, C-N, C-P, C–S, and other bonds; (ii) the ability to achieve highly enantioselective transformations using chiral catalysts and auxiliaries; (iii) conformity with the principle of atom economy; and (iv) usually mild reaction conditions, etc. An extensive synthetic potential of the Michael-type additions stimulated numerous mechanistic studies carried out over the past decades by several research groups [2-6]. However, most of the data available are based on kinetic studies of reaction of α,β -unsaturated electrophilic substrates with amine nucleophiles. Establishment of the mechanism of this reaction was found to be a difficult problem, and alternative mechanistic hypotheses including stepwise and concerted pathways were proposed.

Much less information is available about the mechanism of the phospha-Michael reaction, where tertiary phosphine acts as a nucleophile. To fill up the gap in the theory of the Michael-type additions, we have recently started a systematic study of the mechanism of the reaction of tertiary phosphines

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with unsaturated carboxylic acids and their derivatives [7]. In comparison with amines, phosphines are stronger nucleophiles, but have weaker basic character (e.g., pK_a for the conjugate acid of PPh₃ in water is 2.7 [8]). It makes possible to observe the addition of tertiary phosphines to acidic unsaturated substrates both in acidic and nonacidic solvents and thus to extract from experimental observations more definite information about the mechanism of proton transfers, which accompany most of the Michaeltype reactions. The data obtained for the reaction of tertiary phosphines with activated alkenes allowed us to propose a stepwise mechanism, which includes the reversible formation of zwitterionic intermediate **A**, followed by rate-determining proton transfer to the generated carbanionic center from a proton donor solvent or a second molecule of unsaturated acid (Scheme 2).

When unsaturated carboxylic acid is used as a substrate, and if the addition of tertiary phosphine proceeds in an aprotic solvent, the reaction obeys third-order kinetics, being first order in the phosphine and second order in the unsaturated acid [7d, f]. However, previous conclusions were based on a relatively limited number of the solvents used for the kinetic study. To obtain more detailed information on the mechanism and to find the best model of the solute–solvent interaction to describe the solvent effect on the reaction, it seemed us reasonable to expand the series of previously used aprotic solvents. In this paper, we analyze the results of the kinetic study of the reaction of triphenylphosphine with acrylic acid in a series of 16 aprotic solvents using various well-established one- and multiparameter equations.

EXPERIMENTAL

Materials

All chemicals were obtained from Acros Organics (Geel, Belgium) or Alfa Aesar (Heysham, UK) and were of the highest quality available. Acrylic acid was redistilled under reduced pressure in the presence of small amounts of hydroquinone immediately before use. Triphenylphosphine was used without additional purification. The solvents were purified at the day of use according to known [9] or slightly modified procedures.

Ethylene carbonate and propylene carbonate were redistilled under reduced pressure. Acetonitrile and ethyl formate were distilled over CaH₂.

Propionitrile was shaken twice with 5-mL portions of concentrated hydrochloric acid for 5 min. Then it was shaken with saturated potassium carbonate solution, and the mixture was allowed to

$$PR_3 + \swarrow EWG \xrightarrow{k_1}_{k_{-1}} R_3P \xrightarrow{\oplus}_{A\Theta} EWG$$



EWG = CO₂H, CO₂Me, CN, CONH₂; solvent: AcOH



RDS = rate-determining step

SCHEME 2 Proposed mechanism for addition of tertiary phosphines to activated alkenes.

stand over anhydrous sodium sulfate for several days. Thereafter, the solvent was decanted, distilled from P_2O_5 and, finally, from CaH₂.

Sulfolane was vacuum distilled twice from solid potassium hydroxide and, finally, from CaH₂. Ethyl acetate, butyl acetate, methyl acetate, and diethyl carbonate were dried over 4 Å molecular sieves and distilled.

Tetrahydrofuran (THF), 1,4-dioxane, 1,3dioxolane, and 1,2-dimethoxyethane were purified by the same procedure as follows: Initially, the solvent was distilled from benzophenone ketyl in argon atmosphere. To remove traces of peroxides, the distillate was then treated with triphenylphosphine (\sim 2 g/L), and the solution was allowed to stand at room temperature under argon overnight. Finally, the solution was fractionally distilled under reduced pressure in argon atmosphere. *N*,*N*-Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were dried over 4 Å molecular sieves and distilled under reduced pressure.

The purity of all compounds was confirmed by boiling or melting points and refractive indexes. The solvent purity was additionally verified by the absence of the changes in the spectra of the prepared solution of triphenylphosphine throughout a day.

Kinetics

All kinetic data were obtained spectrophotometrically on a Perkin-Elmer Lambda 35 UV/vis spectrometer with 1 cm, thermostated $(\pm 0.1^{\circ}C)$, quarts cells within a general temperature interval 10-70°C, corrected for each solvent according to its melting or boiling point (for details, see Fig. 2). The reaction was studied under pseudo-first-order conditions, in which the acrylic acid concentration was at least 100 times greater than the concentration of triphenylphosphine, $[PPh_3] \sim 10^{-4}$ M. The reaction was followed by monitoring the decrease in the absorbance of triphenylphosphine at $\lambda = 300$ nm to over 80% completion. The pseudo-first-order rate constants k' were determined from the slope of the plot (R > 0.9998) ln($A_x - A_\infty$) versus time *t*, where A_x and A_{∞} are the measured absorbances at time *t*, and completion of the reaction, respectively. Standard deviations in k' in individual runs were less than 3%. The third-order rate constants $k_{\rm III}$ were obtained from the slope of a plot (R > 0.999) k' versus [acrylic acid]² with \geq 5 concentrations. Activation parameters were calculated from standard Arrhenius plots (R > 0.9995) with seven different temperatures, values of ΔH^{\pm} and ΔS^{\pm} are within $\pm 2 \text{ kJ mol}^{-1}$ and ± 7 J mol⁻¹ K⁻¹, respectively. Examples of the

SCHEME 3 Reaction of triphenylphosphine with acrylic acid in aprotic solvents.



SCHEME 4 Self-association of acrylic acid in its own solutions and in non- and weakly basic solvents.

kinetic methodology are given in the Supporting Information.

Regression Analysis

The regression analysis was carried out using Origin and Microsoft Excel computer software. The quality of correlations was estimated on the basis of correlation coefficient *R* and standard deviation *s*. According to IUPAC recommendations, a correlation was regarded as acceptable when $R \ge 0.95$ [10].

RESULTS AND DISCUSSION

For practical reasons, triphenylphosphine and acrylic acid were found to be the most easy-to-use reactants to study the solvent effect on the kinetics of the addition of tertiary phosphines to unsaturated carboxylic acids (Scheme 3).

From viewpoint of the reaction mechanism, this choice of reactants, as will be shown later, is not crucial. However, it is advantageous that the rate of chosen reaction is within the range suitable for the experimental measurement for a wide series of solvents, and pseudo–first-order condition in the phosphine can be excellently complied. Another advantage is that there is no restriction in solubility of substrates in solvents of different classes. The use of the monocarboxylic acid is also preferred, since it allows to avoid the complication of the reaction kinetics due to appearance of the parallel channels of proton transfer, as observed for the dicarboxylic acids [7a].

However, there are a number of restrictions that complicate the application of some solvents for the kinetic study. The ability of carboxylic acids to self-associate via intermolecular hydrogen bonding (Scheme 4) limits the use of non- and weakly basic solvents, such as hydrocarbons and halogenated hydrocarbons.

Acrylic acid associated with a solvent or a second molecule of acrylic acid behaves differently in the addition step (that reflects on k_1/k_{-1}) and the protonation step (that reflects on k_2). If the solvent is not able to specific solvation of the acid, the equilibrium in solution is not shifted exclusively toward the acid associated with this solvent, and the reaction shows very complex kinetics, as observed for hydrocarbons and their halogenated derivatives. Simplification of the reaction kinetics in this case could be achieved using highly diluted solutions of acrylic acid, [acrylic acid] \rightarrow 0; however, such a situation becomes impossible under the pseudo-first-order condition in the phosphine that requires [acrylic acid] >> [PPh₃]. However, the problem of self-association of acrylic acid can be solved by application of proton acceptor solvents; these were used in our study.

Moreover, it should be noted that the use of acyclic monoethers, such as Et_2O and n- Bu_2O , is impossible due to insolubility of the reaction product. Ketones are not appropriate solvents for spectrophotometric measurements because of their absorption at the operating wavelength of 300 nm.

Despite the above restrictions, the scope of solvents suitable for the kinetic study remains sufficiently broad; this allowed us to expand considerably the series of seven aprotic solvents used previously [7d] by adding ethylene carbonate, propylene carbonate, methyl acetate, ethyl formate, propionitrile, 1,4-dioxane, 1,3-dioxolane, 1,2-dimethoxyethane, and THF.

Kinetic Equation and Reaction Mechanism

As previously described, clear nonlinear dependences of the pseudo–first-order rate constant k' on the concentration of acrylic acid in the aprotic solvent were found (examples for ethylene carbonate and propylene carbonate are given in Fig. 1A), and a plot of log k' versus log[acrylic acid] gives a slope close to 2, indicating that the reaction is second order in acrylic acid (Fig. 1B). Thus, the third-order kinetic equation (1) is general for the reaction of acrylic acid with triphenylphosphine carried out in any aprotic solvent, if the kinetics is not complicated by self-association of the acid in solution, as mentioned above.

Rate =
$$\frac{k_1}{k_{-1}} k_2 [PPh_3] [acrylic acid]^2$$

= $k_{III} [PPh_3] [acrylic acid]^2$ (1)

where $k_{\text{III}} = k_1 k_2 / k_{-1}$ is the third-order rate constant.

It is noteworthy that a comparison of the kinetic parameters strongly suggests that the reaction involves an identical mechanism for all the aprotic solvents used. For example, an isokinetic plot of $\log k_{\text{III}}^{T+30}$ versus $\log k_{\text{III}}^T$, also known as the Exner criterion [11], exhibits the excellent linear character, as shown in Fig. 2 and Eq. (2).

$$\log k_{\text{III}}^{T+30} = (0.901 \pm 0.012) \log k_{\text{III}}^{T} + (0.416 \pm 0.030)$$

N= 16, R= 0.99975, s= 5.04 × 10⁻⁴ (2)

where k_{III}^T and k_{III}^{T+30} are third-order rate constants at temperatures *T* and *T*+30, respectively.

Interestingly, Eq. (2) is identical to those ones obtained previously for the same reaction carried out in protic solvents (alcohols and carboxylic acids [7c]) and for the similar reactions with other activated alkenes [7h] and tertiary phosphines [7f]. Therefore, solvents and substituents do not have a primary effect on the energy surface (i.e., do not change the rate-determining step and the structure of the intermediate), and following conclusions about the mechanism of the reaction of triphenylphosphine with acrylic acid are valid for other examples of this type of phospha-Michael reaction.

Two main conclusions about the mechanism follow from the kinetic equation (1); they are in accordance with our previous observations:

- (i) The rate-determining step is the proton transfer, and this is not a function of solvent properties (e.g., basicity and/or polarity);
- (ii) The proton transfer proceeds exclusively via a intermolecular pathway with assistance of a second proton donor molecule (in this case, the second molecule of acrylic acid).

Since the rate-determining protonation of the carbanionic center in acidic media seems quite surprising, it was important for us to demonstrate in the current study the generality of this mechanism for a wide series of solvents. Recently, we also attracted additional experimental and theoretical facts [7g] to support this mechanistic proposal. The data obtained allowed us to conclude that such a mechanism is the result of high lability of the phosphonium zwitterion, whereby the decomposition rate k_{-1} becomes much greater than the rate of proton transfer k_2 (Scheme 2). The attempts to explain the reaction mechanism without assignment of the ratedetermining step to the protonation of carbanionic center are not satisfactory, and most realistic ones are presented below.

One can assume that the second molecule of acrylic acid becomes involved in the reaction



FIGURE 1 Plots of *k* versus [acrylic acid] (A) and log *k* versus log [acrylic acid] (B) for the reaction of triphenylphosphine with acrylic acid in aprotic solvents at 30°C (for ethylene carbonate, at 40°C). (a) propylene carbonate: log k + 1 = 1.88 log[acrylic acid] - 1.114 ($R^2 = 0.9999$, y = 1); (b) ethylene carbonate: log k = 1.90 log[acrylic acid] - 0.777 ($R^2 = 0.9999$, y = 0); (c) propionitrile: log k = 1.90 log[acrylic acid] - 1.319 ($R^2 = 0.9988$, y = 0); (d) ethyl formate: log k = 1.80 log[acrylic acid] - 1.987 ($R^2 = 0.9992$, y = 0); (e) 1,3-dioxolane: log k - 0.2 = 2.09 log[acrylic acid] - 1.960 ($R^2 = 0.9993$, y = -0.2); (f) methyl acetate: log k - 0.5 = 1.98 log[acrylic acid] - 2.009 ($R^2 = 0.9995$, y = -0.5); (g) 1,4-dioxane: log k = 2.09 log[acrylic acid] - 2.781 ($R^2 = 0.9996$, y = 0); (h) THF: log k = 2.09 log[acrylic acid] - 3.139 ($R^2 = 0.9996$, y = 0); (i) 1,2-dimethoxyethane: log k - 1 = 2.07 log[acrylic acid] - 2.702 ($R^2 = 0.9998$, y = -1).



FIGURE 2 Isokinetic plot of $\log k_{\rm III}^{T+30}$ versus $\log k_{\rm III}^T$ for the reaction of triphenylphosphine with acrylic acid in aprotic solvents (T = 283 K for acetonitrile, ethyl formate, 1,3-dioxolane, methyl acetate, ethyl acetate, 1,2-dimethoxyethane, THF; T = 293 K for propionitrile, diethyl carbonate, butyl acetate, DMF, DMSO; T = 294 K for 1,4-dioxane; T = 298 K for propylene carbonate, T = 303 K for sulfolane; T = 313 K for ethylene carbonate). For solvent numbering, see Table 1.

mechanism as a result of general- or specific-acid catalysis, in which the first molecule of the acid protonates the second one at the carbonyl oxygen atom and, thus, increases the electrophilicity of the C=C bond in the latter molecule. According to the wellknown theory of acid-base catalysis [12], the scenario of general acid catalysis requires the involvement of the proton transfer in the rate-determining step; this step would have occurred here prior the attack of the phosphine (Scheme 5). As a result, the kinetic equation would have form (3) with the zero order in the phosphine that contradicts the experimental observations.

$$Rate = k_{obs} [Acrylic Acid]^2$$
(3)

The scenario of the specific-acid catalysis, presented in Scheme 6, would result in a kinetic equation (4), which is also inconsistent with the experimental data, because for a weak acrylic acid the following expression is true: $[H^+] =$ $= \sqrt{K_{\text{dis}}[\text{acrylic acid}] \neq [\text{acrylic acid}]$ (where K_{dis} is a dissociation constant of acrylic acid in a given solvent):

$$Rate = k_{obs}[PPh_3][Acrylic Acid][H^+]$$
(4)

The third-order kinetic equation (1) could be explained in terms of hydrogen bonding between two molecules of acrylic acid with only partial protonation of the carbonyl oxygen atom followed by the rate-determining addition of the phosphine (Scheme 7).

However, it seems doubtful that such partial protonation can significantly increase the electrophilicity of the terminal carbon atom of the C=C bond in comparison with the non-hydrogen bonded acrylic acid (i.e., to make $\Delta + >> \delta +$; Scheme 7); the non-hydrogen bonded acrylic acid must be considered as unreactive in this scenario to provide "pure" second-order kinetics in the acid. Moreover, the solvent effect on this reaction, as will be seen later,



SCHEME 5 The general-acid-catalyzed reaction scenario.



SCHEME 6 The specific-acid-catalyzed reaction scenario.



SCHEME 7 The reaction scenario involving hydrogen bonding between two molecules of acrylic acid.

definitely requires the proton transfer to be the ratedetermining step.

One more possible scenario involves the generation of a low-polarity prereaction complex **C** between the phosphine and acrylic acid, in which the formation of covalent P–C bond proceeds relatively synchronous with the proton transfer to the incipient carbanionic center from a second molecule of acrylic acid (Scheme 8). However, the strong substituent effect [7f, h] and solvent effect (see below) forced us to abandon such a concerted mechanism, considered as the most likely in our initial reports [7a-c].

The absence of intramolecular proton migration within the zwitterionic intermediate **A** (EWG = CO_2H) (Scheme 2), as follows from the kinetic equation (1), is also quite remarkable. Now we can summarize that it is a general phenomenon for all types of solvents, both aprotic and protic ones [7c, h]. The quantum chemical calculations, carried out for a model reaction in the gas phase showed [7g] that the involvement of a second



SCHEME 8 The reaction scenario involving the low-polarity prereaction complex between triphenylphosphine and acrylic acid.

TABLE 1 Kinetic and Activation Parameters for the Reaction of Triphenylphosphine with Acrylic Acid in Aprotic Solvents (30°C)

Entry	Solvent	10 ³ k_{III} ($M^{-2} s^{-1}$)	ΔH^{\neq} (kJ mol ⁻¹)	$-\Delta S^{\neq}$ (J mol ⁻¹ K ⁻¹)	Reference
1	Ethylene carbonate	(143) ^a	27.4	171	This work
2	Propylene carbonate	93.1 ± 1.1	29.1	169	This work
3	Acetonitrile	56.9 ± 0.7^{b}	29.3	172	[7d]
4	Propionitrile	55.2 \pm 0.7	29.2	173	This work
5	Sulfolane	$40.3~\pm~0.5$	32.4	165	[7d]
6	Diethyl carbonate	$25.4~\pm~0.5$	31.3	173	[7d]
7	Ethyl formate	13.2 \pm 0.2	36.7	160	This work
8	1,3-Dioxolane	10.7 \pm 0.3	36.9	161	This work
9	Butyl acetate	10.6 \pm 0.05	35.7	165	[7d]
10	Methyl acetate	$9.83~\pm~0.05$	31.9	178	This work
11	Ethyl acetate	$9.14~\pm~0.04$	34.0	172	[7d]
12	1,2-Dimethoxyethane	$2.03~\pm~0.03$	39.1	168	This work
13	1,4-Dioxane	$1.67~\pm~0.02$	39.0	169	This work
14	THF	$0.742~\pm~0.009$	42.5	165	This work
15	DMF	$0.138~\pm~0.005$	47.8	161	[7d]
16	DMSO	$0.081~\pm~0.004$	43.5	180	[7d]

^aValue extrapolated from 40–70°C temperature interval.

^bRefined value compared with the previously reported [7d].

proton donor molecule in the reaction is a result of kinetic forbiddance for intramolecular proton transfer via four-membered cyclic transition state **B** (Scheme 2). Evidently, this tendency is valid when the gas phase is replaced by any solvent. Interestingly, the four-membered cyclic transition state for a proton transfer was proposed for the Michaeltype reaction of primary and secondary amines with activated alkenes [5], but the reaction mechanism remains controversial [4d]. For the phospha-Michael reaction of tertiary phosphines with activated alkenes, the third-order kinetic equation allows us to explicitly exclude a similar cyclic transition state from the mechanism.

Solvent Effect on the Reaction Kinetics

The influence of the solvent on the kinetic and activation parameters of the studied reaction is summarized in Table 1, where both previously and currently obtained data for aprotic solvents were collected for convenience.

As follows from Table 1 with the rate constants varying over a 1500-fold range, the reaction is very sensitive to the solvent effect. The strong solvent effect is typical for reactions involving significant redistribution of electron density among the reactants (i.e., having polar intermediates in the pathway) than for reactions involving low-polarity intermediates with partially broken or formed bonds (e.g., complex C from Scheme 8). According to the rate constant k_{III} , aprotic solvents can be roughly divided into three groups. The first group consists of "fast" solvents ($k_{\rm III} > 3 \times 10^{-2} \text{ M}^{-2} \text{ s}^{-1}$), such as ethylene and propylene carbonates, nitriles, and sulfolane. Notably, this group contains solvents with weak basic characteristics and sufficiently large dielectric constants (Table 2). Such solvents may be recommended for this type phospha-Michael reaction. The second group of solvents with "medium" rates $(3 \times 10^{-4} \le k_{\text{III}} \le 3 \times 10^{-2} \text{ M}^{-2} \text{ s}^{-1})$ contains esters (except for ethylene and propylene carbonates) and ethers. As compared with the first group of solvents, esters of this group have much smaller dielectric constants but possess approximately the same basic properties (Table 2). Polarity and basicity of ethers are very varied and depend on the structure of carbon chain (cyclic or acyclic) and relative position of oxygen atoms. If a series of ethers with very similar dielectric constants is considered, 1,3dioxolane-1,2-dimethoxyethane-THF, one can notice that the reaction rate slows down as the solvent basicity increases (Table 1). DMF and DMSO belong to the third group of "slow" solvents ($k_{\rm III} < 3 \times 10^{-4}$

Solvent	ε [9]	n [9]	<i>E</i> _T [13]	Y ^a	P^b	<i>E</i> [14]	B[15]
Ethylene carbonate	89.78	1.4195	48.6	0.4917	0.33665	6.7 ^d	-
Propylene carbonate	64.92	1.4215	46.0	0.4885	0.33789	4.3 ^d	176 ^{<i>e</i>}
Acetonitrile	35.94	1.3441	45.6	0.4794	0.28740	5.2	160
Propionitrile	28.86	1.3658	43.6	0.4745	0.30202	3.2	162
Sulfolane	43.26	1.4833	44.0	0.4829	0.37503	2.3	157
Diethyl carbonate	2.82	1.3851	36.7	0.2741	0.31472	3.7 ^d	145
Ethyl formate	7.16	1.3599	40.9	0.4021	0.29808	3.7 ^d	185 ^{<i>e</i>}
1,3-Dioxolane	6.98 ^c	1.3992	43.1	0.3997	0.32381	5.8 ^d	196
Butyl acetate	5.01	1.3942	38.5	0.3639	0.32060	2.6 ^d	158
Methyl acetate	6.68	1.3614	38.9	0.3955	0.29908	2.0^{d}	170
Ethyl acetate	6.02	1.3724	38.1	0.3850	0.30639	1.6	181
1,2-Dimethoxyethane	7.20	1.3796	38.2	0.4026	0.31113	0	238
1,4-Dioxane	2.209	1.4224	36.0	0.2231	0.33845	4.2	237
THF	7.39	1.4076	37.4	0.4049	0.32916	0	287
DMF	36.71	1.4305	43.2	0.4798	0.34347	2.6	291
DMSO	46.45	1.4793	45.1	0.4840	0.37271	3.2	362

TABLE 2 Solvent Parameters Used in the Koppel–Palm Equation

^aCalculated by Eq. (17).

^bCalculated by Eq. (19).

^cTaken from [16].

^dCalculated by Eq. (20). ^eData obtained from Prof. G. Midvana.

 $\rm M^{-2}~s^{-1}$). Apparently, high polarity is incapable of compensating strong deceleration of the rate as a result of very high basicity of these solvents. For synthetic purposes, the use of solvents from the third group should be avoided in the phospha-Michael reaction.

The activation parameters presented in Table 1 give interesting information about the reaction intermediate. As seen from Table 1, the values of entropy of activation are always very negative and for this reason the ΔS^{\neq} term contributes significantly to the Gibbs free energy of activation ($\Delta G^{\neq} = \Delta H^{\neq} - T \Delta S^{\neq}$) at ambient temperatures. Large negative values of the ΔS^{\neq} are typical for reactions involving polar intermediates and usually arise from solvation effects, viz. electrostriction of the solvent [13], the ordering of polar solvent molecules around the charged centers appearing in the reaction pathway. However, one can notice that the ΔS^{\neq} values do not increase as the polarity of solvent increases (e.g., compare the ΔS^{\neq} values for low-polarity 1,4-dioxane and highly polar propylene carbonate; see Table 1). Taking into account the experimental error in the determination of ΔS^{\neq} ($\pm 7 \text{ Jmol}^{-1} \text{ K}^{-1}$), the reaction series may be regarded as isoentropic; this leads to the general isokinetic plot shown in Fig. 2. The assignment of large negative values of entropy of activation to the electrostriction of the solvents in such a situation is doubtful. Most probably, these ΔS^{\neq} values are a result of highly organized structures of the reaction intermediate and transition states themselves that require rigorous arrangement of reactants relative to each other for the efficient P-C and C-H bonds

formation. We can speculate that the absence of electrostriction is a result of high lability of the zwitterionic intermediate **A**, which reconverts to the starting materials or transforms to the reaction product with very large rate constants k_{-1} and k_2 , respectively. The lifetime of this zwitterions is not long enough to produce ordering of polar solvent molecules around the separated charges.

To obtain further information on the reaction mechanism, we analyzed the solvent effect using a linear free energy relationship on the basis of different empirical models of solute-solvent interactions. The attempts to correlate the reaction rate with only one solvent parameter were not satisfactory, suggesting that different specific and nonspecific interactions contribute to the ΔG^{\neq} of this reaction. To achieve correlations of better quality, multiparameter equations were applied. It should be noted that we knowingly did not use the opportunity to improve the quality of the correlations by exclusion the most deviating points for some of the solvents, since the presence of the general isokinetic plot (Fig. 2, Eq. (2)) discredits such efforts. The only reason why not all of the solvents were used in a correlation was the lacking of a solvent parameter in the literature. The solvent parameters of the Koppel–Palm equation are given in Table 2, and other solvent parameters used in this study are presented in the Supporting Information. The results of one- and multiparameter regression analysis are summarized in Table 3.

As follows from Table 3, there is only a weak positive correlation between the reaction rate and the solvent polarity, defined either as the Kirkwood

TABLE 3 Results of (One- and Multiparameter Regression Analysis of the Solvent Effect on the Ri	late of the Rea	ction of Triphenylphosphine with Acrylic A	bid
Model	Result of Full Correlation	Equation	Result after Exclusion of Statistically Insignificant Parameters	Equation
Kirkwood function [17]	$\log k_{\rm III} = -2.72 + (1.5 \pm 6.9) Y$ $N = 16, R = 0.121, s = 0.981$	(5)		
Reichardt parameter [13]	log $k_{\rm HII} = -5.3 + (7.7 \pm 14) \times 10^{-2} E_{\rm T}$ N = 16, R = 0.309, s = 0.900	(9)		
Kamlet–Taft equation [18, 19]	log $k_{ m lll} = 0.28 + (1.4 \pm 1.9)\pi * + (2.3 \pm 6.1)lpha - (7.6 \pm 2.9)eta$ N = 15, R = 0.883, s = 0.245	(7)	$\log k_{ m III} = 0.85 - (6.6 \pm 2.6) eta$ N = 15, R = 0.836, s = 0.283	(12)
Catalán equation [20]	log $k_{\text{III}} = 2.8 - (2.0 \pm 6.7)$ SPP + (0.63 \pm 1.9)SA - (6.9 \pm 3.4)SB N = 13, R = 0.862, s = 0.334	(8)	$\log k_{\rm HI} = 1.0 - (6.8 \pm 2.8) \rm SB$ N = 13, R = 0.845, s = 0.304	(13)
Gutmann–Mayer equation [21]	log $k_{\text{III}} = 0.12 + (7.7 \pm 6.7) \times 10^{-2}$ AN $- (18.9 \pm 5.8) \times 10^{-2}$ DN $N = 11, R = 0.939, s = 0.169$	(6)	log $k_{\rm HI} = 1.2 - (18.7 \pm 6.8) \times 10^{-2} \rm DN$ N = 15, R = 0.855, s = 0.288	(14)
Koppel–Palm equation [17,22]	$ \begin{array}{l} \log k_{\rm HI} = -0.57 + (2.1 \pm 2.5) Y + (0.66 \pm 8.7) P + \\ + (5.8 \pm 12) \times 10^{-2} E - (1.39 \pm 0.37) \times 10^{-2} B \\ N = 15, R = 0.958, s = 0.102 \end{array} $	(10)	$\log k_{\rm HI} = -0.14 + (2.2 \pm 2.3) Y(1.42 \pm 0.29) \times 10^{-2} B$ N = 15, R = 0.952, s = 0.095	(15)
	log $k_{ m III} = -1.7 + (6.0 \pm 4.7) imes 10^{-2} E_{ m T} - (1.40 \pm 0.26) imes 10^{-2} B$ N = 15, R = 0.961, s = 0.078	(11)	log $k_{\rm HI} = 6.6 - (1.38 \pm 0.31) \times 10^{-2}B$ N = 15, R = 0.935, s = 0.119	(16)



function (Eq. (17) [17]), or the Reichardt parameter $E_{\rm T}$ [13], as confirmed by very low coefficients of the pair correlations: 0.121 and 0.309, respectively (Eqs. (5) and (6); Table 3).

$$Y = \frac{\varepsilon - 1}{2\varepsilon + 1} \tag{17}$$

where ε is a dielectric constant.

However, there are strong negative correlations (0.8 < R < 0.95) with the solvent basicity expressed in any of the scales used (i.e., DN, β , SB, B, see Eqs. (12)—(14) and (16) and Table 3). The Kamlet-Taft and the Catalán multiparameter equations do not describe satisfactory the solvent effect; even if the parameters responsible for solvent dipolaritypolarizability (π^* , SPP) and Lewis acidity (α , SA) are included into correlations, the correlation coefficient remains less than 0.9 (Eqs. (7) and (8); Table 3). The Gutmann-Mayer equation based on the donor numbers (DN) as a measure of the Lewis basicity of the solvent and the acceptor numbers (AN) as a measure of the Lewis acidity of solvent allows to achieve better correlation (R = 0.939, Eq. (9), Table 3), but it still cannot be regarded as satisfactory. The Koppel-Palm equation was found to be a more appropriate model to describe the solvent effect.

In the Koppel–Palm model, the total solvent effect on a reaction rate is determined by the fourparameter equation (18) [17].

$$\log k = \log k_0 + yY + pP + eE + bB \tag{18}$$

where polarity *Y* and polarizability *P* describe nonspecific components of solute–solvent interactions; electrophilicity/acidity *E* and nucleophilicity/basicity *B* describe specific components of these interactions; *y*, *p*, *e*, *b* characterize the sensitivity of a given reaction toward the corresponding solvation effect; k_0 formally conforms to rate constant in the gas phase.

The polarity *Y* is the Kirkwood function; the polarizability *P* is defined by Eq. (19):

$$P = \frac{n^2 - 1}{n^2 + 1} \tag{19}$$

where *n* is the refractive index.

The electrophilicity/acidity E is expressed by the Reichardt parameter $E_{\rm T}$, improved by subtraction of the nonspecific interaction in accordance with Eq. (20).

$$E = E_T - 25.10 - 14.84 \frac{\varepsilon - 1}{\varepsilon + 2} - 9.59 \frac{n^2 - 1}{n^2 + 2}$$
(20)

The nucleophilicity/basicity B is based on the shift of the OH stretching vibration of phenol within the complex with a solvent molecule in

tetrachloromethane solution and phenol in tetrachloromethane solution (Eq. (21)).

$$B = \Delta \bar{v}_{\text{PhOH}}^{\text{CC1}_4} = \bar{v}_{\text{PhOH}}^{\text{CC1}_4} - \bar{v}_{\text{PhOH-Solv}}^{\text{CC1}_4}$$
(21)

The correlation coefficient for the full, fourparameter Koppel–Palm regression is 0.958 (Eq. (10), Table 3). The exclusion of the statistically insignificant *P* and *E* parameters gives Eq. (15) (Table 3) with satisfactory R = 0.952. Although the parameter *Y* in Eq. (15) is also weakly significant, the exclusion of this parameter leads to oneparameter correlation (16) (Table 3) with unsatisfactory R = 0.935. Therefore, the success of the Koppel– Palm equation compared with other multiparameter equations is mainly a result of a very strong correlation of the rate constants with the parameter *B*.

Further improvement of the quality of correlation can be achieved by using the Reichardt parameter E_T instead of the *Y*, *P*, and *E* parameters (R = 0.961, Eq. (11), Table 3). Such transformation seems reasonable, since the use of procedure described by Eq. (20) makes the *E* parameter less reliable than the E_T parameter [23].

Presented quantitative analysis of the solvent effect on the reaction rate is a good evidence to the mechanism proposed in Scheme 2. An obvious considerable impact of the solvent basicity on the reaction rate proves the assignment of the ratedetermining step to the proton transfer. A pronounced decrease in the reaction rate with the increase in the solvent basicity can be assigned to the double negative effect of this parameter on the rate constant $k_{\text{III}} = k_1 k_2 / k_{-1}$. The solvent basicity not only decreases the protonation rate k_2 but also retards the nucleophilic attack of the phosphine k_1 , since hydrogen bond with a proton acceptor solvent stabilizes the ground state of acrylic acid and reduces the electron-withdrawing effect of the carboxyl group attached to the C=C bond. Therefore, the attempts to accelerate reaction using highly polar solvents to make smaller the decomposition rate k_{-1} are failed. when the solvent possesses highly basic properties, as observed for DMF and DMSO.

From viewpoint of the proposed reaction mechanism, the polarity of the solvent expressed either in the *Y* or the E_T scale favors the reaction due to more efficient stabilization of the zwitterionic intermediate **A** and reduction of the decomposition rate k_{-1} (positive signs before these parameters in Eqs. (11) and (15)). Such additional stabilization can be achieved both by a dipole–dipole interaction with the solvent and an interaction of the solvent as a Lewis acid with the anionic moiety of the intermediate. Evidently, the "overall solvation" E_T parameter describes better the interaction of the solvent with



FIGURE 3 The relationship between experimental and calculated rate constants on the basis of correlation Eq. (11) (for solvent numbering, see Table 1).

this zwitterion than it does the Kirkwood function Y (or free of nonspecific contribution, the parameter E).

Most probably, the small statistical significances of the Y and $E_{\rm T}$ parameters in Eqs. (11) and (15) come from high lability of the reaction intermediate; its very short lifetime does not allow the solvent to be efficiently involved in the interaction. This assumption is supported by the nearly constant values of the entropy of activation for the solvents with very different polarity, as discussed above.

Thus, Eq. (11) may be regarded as the best-fit model to describe the solvent effect. Figure 3 illustrates a satisfactory relationship between the experimental rate constants and those ones calculated by this equation. The presented study allowed us to refine the previous conclusions [7d, f] about the individual contribution of solvent parameters to the overall effect on the reaction rate, when a fewer number of solvents was used.

CONCLUSIONS

The kinetics of the reaction of triphenylphosphine with acrylic acid was studied in a series of aprotic solvents. The rate equation has general third order, first order in the phosphine, and second order in the acid. This equation was interpreted in terms of previously suggested a stepwise mechanism with the initial nucleophilic attack of the phosphine on the terminal carbon atom of the C=C bond of the acid, followed by rate-determining proton transfer to the generated carbanionic center from the second molecule of acrylic acid as shown in Scheme 2. In

this mechanism, the second-order kinetics in the acid arises from one molecule being a reactant with the phosphine and the other as a proton source in the rate-determining step. Alternative mechanistic proposals are also considered, but neither of them are in agreement with the scope of the experimental observations. The reaction rate is very sensitive to the solvent effect; this effect was analyzed using the linear free energy relationship on the basis of the one- and multiparameter equations, such as the Kamlet-Taft, the Catalán, the Gutmann-Mayer, and the Koppel-Palm equations. The results obtained showed that the solvent basicity defined in any of the scales has the dominant and negative effect on the reaction rate, confirming the assignment of the ratedetermining step to the proton transfer. The solvent polarity expressed by the Kirkwood function or the Reichardt $E_{\rm T}$ parameter has only weak positive effect on the rate; this was assigned to extremely labile character of the reaction intermediate that makes solvation effects negligible for this zwitterions. This conclusion is supported by the nearly isoentropic character of the reaction studied in the solvents with different polarities. The combination of the Reichardt $E_{\rm T}$ parameter with the Koppel–Palm basicity parameter B gives a two-parameter equation, which in the best way describes the solvent effect. The presence of the general isokinetic plot makes the conclusions about the reaction mechanism and solvent effects valid for other tertiary phosphines and unsaturated carboxylic acids. The most appropriate aprotic solvents for this phospha-Michael reactions are cyclic carbonates (ethylene carbonate and propylene carbonate), nitriles, and sulfolane due to their weak basic properties and high polarity. The information obtained can be useful for planning similar reactions, where phosphonium zwitterion of type A is involved as a deprotonating agent, for example, phosphine-catalyzed additions of alcohols and CH acids to activated alkenes [24].

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