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Acid-Base Properties of α-Aminomethylphosphine Oxides

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Abstract—Ionization constants of a series of aminomethylphosphine oxides and respective amino precursors, as well as their isostructural amino phosphonates in water–2-propanol or water medium were determined. The main regularities of the effect of the phosphoryl group on the protolytic equilibria involving mono- and bisphosphorylated amines and diamines were found. The environment effect on the ionization constants of hydrophilic aminophosphoryl compounds and amines was estimated quantitatively. The relationship between the dissociation constants of aminophosphoryl compounds and related constants of amino precursors in the framework of the principle of linearity of free energies was demonstrated.

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The rapid development of the chemistry of organophosphorus analogs of natural amino acids, the aminophosphoryl compounds, in recent decades is associated mainly with their high and diverse biological activity stipulating the search for new pharmaceuticals, pesticides, fungicides, and other bioactive compounds among the compounds of this structure [1–3]. However, a variety of practically useful properties of phosphorus compounds of this type are not limited to their bioactivity. In recent years numerous studies have been carried out related to their complexing properties based on their ability to act as mono-, bi- and polydentate ligands. In particular, this valuable property makes it possible to use them as liquid and membrane transporters of natural mono- and polyfunctional organic, inorganic acids and other proton-donor reagents, as well as various metal cations. In addition, they exhibit ionophore properties allowing the preparation of new effective ion-selective electrodes. We have studied previously the extraction and membrane transport properties of lipophilic aminomethylphosphoryl reagents with respect to the carboxylic acids [4–6], ions of alkali, alkaline earth [7], noble [8–11], rare and trace metals [12, 13]. In particular, it was found that they exhibit high efficiency in the extraction of scandium and the possibility of its selective separation from the accompanying elements [14].

To create effective liquid membrane technology with basic reagents as carriers it is necessary to provide the latter with the required hydrophilic–lipophilic characteristics for the optimal interphase distribution. The assessment of such characteristics involves consideration of acid–base properties of the extractants, therefore earlier in a number of papers we have paid attention to exploring this important parameter of the extraction processes. In addition, we suggest that determining the ionization constants is a necessary condition for establishing the *structure–property* relationship for subsequent pre-determined synthesis of transporters and extractants with an optimal set of desired characteristics.

We obtained a large array of pK_a^C values for a significant number of α-amino phosphonates [15–17] and for a limited number of examples of structurally close to them aminophosphine oxides [18]. However, as we have shown on a number of examples [12–14], it is more preferable to use phosphine oxides rather than the aminophosphonate analogs in the processes of extraction and separation of metal ions. This is due to the presence of labile ester bonds in the aminophosphonates that are liable to suffer the hydrolytic and thermal degradation in strongly acidic aqueous media used in the extraction of metals from the mining raw materials. However, as noted above, the information on the acid–base properties of aminoalkylphosphine oxides is limited to a small number of examples.

In this paper we present the data on the acid–base properties in water–2-propanol medium of a large

number of α-aminomethylphosphine oxides and the corresponding amino precursors to assess the effect of the phosphoryl group on these properties.

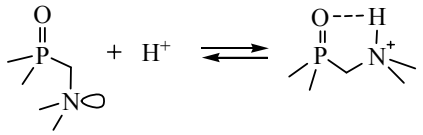
It should be noted that, as mentioned above, the high lipophilicity is one of the most important requirements for the compounds used as industrial extractants, membrane transporters, and ionophores for electrochemical sensors, that is, in the planned areas of practical application of the synthesized and studied by us aminophosphoryl compounds. However, the determination of ionization constants of lipophilic compounds in water involves considerable experimental difficulties, since most of the available methods cannot be used for this purpose due to their extremely low solubility (less than 10^{-4} mol l^{-1}). To study protolytic equilibria in such cases mixed aqueous-organic solvents are widely used. In this paper, as in several our previous experimental studies [15–17], the values of pK_a^C of the conjugate acids of aminophosphine oxides were determined by potentiometric titration of trace substances in the water–2-propanol medium containing 50% water by volume, which ensured a sufficiently high solubility of the studied compounds.

Tables 1 and 2 list the pK_a^C values of the conjugate acids of α-aminomethylphosphine oxides **I–XIV**, *N,N*-(diphosphorylmethyl)octylamines **XV** and **XVI**, and α,α'-di(phosphorylmethyl)diamines **XVII–XXII**. To assess the influence of dialkylphosphoryl groups on the basicity of amines we measured under the same experimental conditions the ionization constants of aliphatic and aromatic amines and diamines, the α-aminomethylphosphine oxide precursors used in the three-component Kabachnik–Fields reaction with the respective phosphinous acids and formaldehyde (Table 3).

Analysis of the effect of the aminophosphoryl compounds structure on their basicity in the investtigated series allows us a conclusion on some general regularities relating the structure and acid–base characteristics of the studied lipophilic α-aminomethylphosphine oxides.

Note that we have found previously that the variation of the substituents at the nitrogen and phosphorus atoms has very little effect on the basicity of the phosphorylated amines, and the pK_a^C values of their conjugate acids are 4–5 units less than the corresponding values of their precursors, the nonphosphorylated amines [16–18]. This pattern is also evident in a series of the studied in this paper α-aminomethylphosphine oxides with aliphatic and aromatic substituents at the nitrogen atom: the difference in the pK_a^C values of the amine and the corresponding α-aminomethylphosphine oxide is about 4 and 5 units for the primary and secondary amines (Table 4) . Such change in the basicity of amines at phosphorylation is quite understandable, given the significant electron-witdrawing effect of the phosphoryl group [19]. In this sense, the fact is very indicative that we were not able to determine the exact values of pK_a^C of the bis-phosphorylated amines **XV** and **XVI**, as in the titration conditions used by us we could not achieve the required proportion of the protonated forms of these compounds. The contribution of the second methylene-phosphoryl group is obviously the same as at the monophosphorylation, and we can assume that the pK_a^C values of the bis-phosphorylated amines should not exceed the value of 1.7. An indirect confirmation of this assumption we obtained in the study of the extraction properties of these compounds: the extraction isotherms of perchloric, nitric and hydrochloric acids reach the limit only at a high concentration of the transported acid [13].

Phosphorylated tertiary amines are much weaker bases than the analogs with secondary nitrogen atom (Table 5). We observed a similar pattern in the study of the acid–base properties of α-amino phosphonates [16]. This is probably due to the repulsion of the dipoles of polar P→O and C→N bonds in the molecules of aminophosphoryl compounds with a tertiary nitrogen atom resulting in the preferred trans-orientation of the nitrogen and the phosphoryl oxygen atoms (structure **A**).



A **B**

The process of protonation of these compounds is expected to be accompanied by a conformational *trans-cis* transition with the formation of an intramolecular hydrogen bond in the H-complex **B**. Such a transition should not occur in the case of the secondary phosphorylamines containing the phosphoryl oxygen and nitrogen atoms already involved in the hydrogen bonding [1, 20], which contributes to the increase in the basicity.

We also determined the ionization constants of *N,N*'-bisphosphoryldiamines, the derivatives of 1,4-diaminobutane **XVII** and 2-methyl-1,5-diaminopentane **XVIII**, 1,6-diaminohexanes **XIX** and **XX**, and

Table 1. Ionization constants (pK_a) of conjugate acid of α-aminomethylphosphine oxides in aqueous (50 vol %) 2-propanol, 298±0.2 K

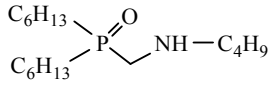
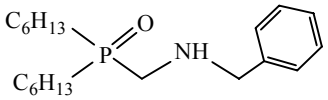
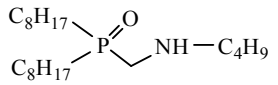
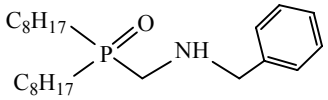
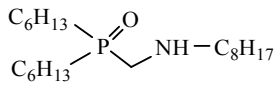
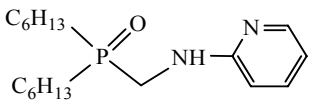
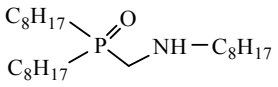
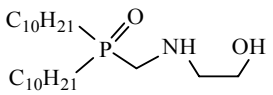
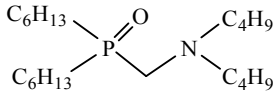
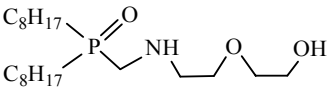
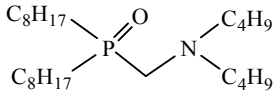
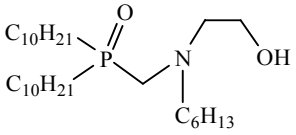
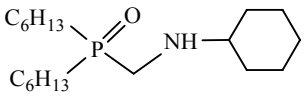
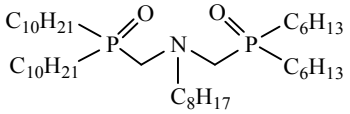
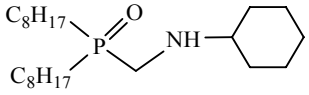
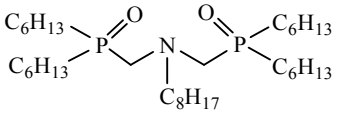
Comp. no.	Compound	pK_a^C ± 0.05	Comp. no.	Compound	pK_a^C ± 0.05
I		5.61	**IX**		4.39
II		5.65	**X**		4.39
III		5.24	**XI**		6.11
IV		5.24	**XII**		5.18
V		4.47	**XIII**		5.09
VI		4.34	**XIV**		3.90
VII		5.52	**XV**		<2
VIII		5.56	**XVI**		<2

Table 2. Ionization constants (pK_a^C) of conjugate acids of α,α-bis(diphosphorylmethyl)diamines in aqueous (50 vol %) 2-propanol, 298±0.2 K

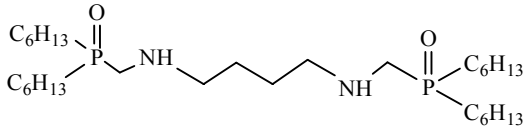
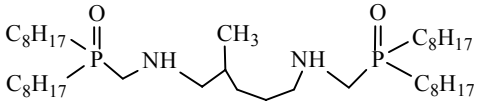
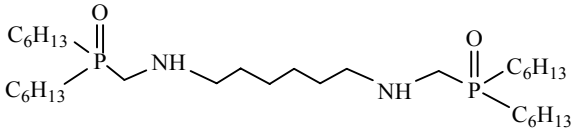
Comp. no.	Compound	pK_a^C ± 0.05
XVII		pK_{a1} 4.04 pK_{a2} 5.61
XVIII		pK_{a1} 4.93 pK_{a2} 5.25
XIX		pK_{a1} 5.38 pK_{a2} 5.70

Table 2. (Contd.)

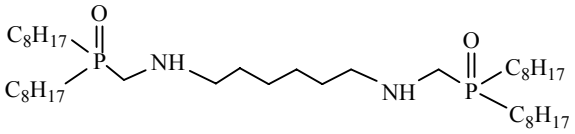
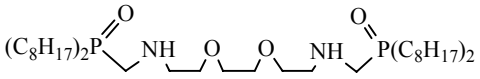
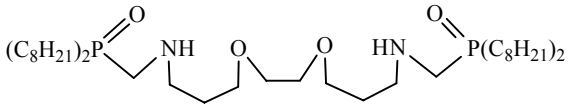
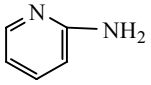
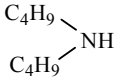
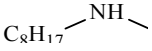
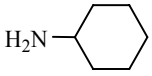
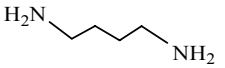
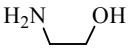
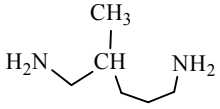
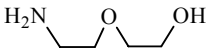
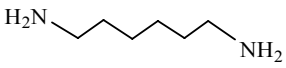
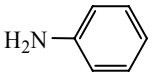
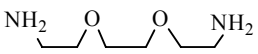
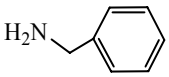
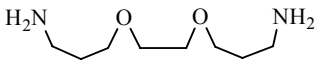
Comp. no.	Compound	$pK_a^C \pm 0.05$
XX		pK_{a1} 5.42 pK_{a2} 5.90
XXI		pK_{a1} 4.30 pK_{a2} 5.25
XXII		pK_{a1} 5.17 pK_{a2} 5.79

Table 3. Ionization constants (pK_a^C) of amines in aqueous (50 vol %) 2-propanol, 298±0.2 K

Comp. no.	Amine	$pK_a^C \pm 0.05$	Comp. no.	Amine	$pK_a^C \pm 0.05$
XXIII	$H_2N–C_4H_9$	9.74	**XXXI**		6.19
XXIV	$H_2N–C_6H_{13}$	9.68	**XXXII**		9.60
XXV	$H_2N–C_8H_{17}$	9.49	**XXXIII**		8.98
XXVI		9.55	**XXXIV**		pK_{a1} 8.28 pK_{a2} 9.85
XXVII		9.00	**XXXV**		pK_{a1} 8.85 pK_{a2} 9.74
XXVIII		8.85	**XXXVI**		pK_{a1} 9.08 pK_{a2} 10.06
XXIX		3.99	**XXXVII**		pK_{a1} 8.20 pK_{a2} 8.98
XXX		8.42	**XXXVIII**		pK_{a1} 8.28 pK_{a2} 9.12

two *N,N'*-bisphosphorylated diazapodands, the derivatives of 1,8-diamino-3,6-dioxaoctane **XXI** and 1,10-diamino-4,7-dioxadecane **XXII**. Two latter, as we have previously shown [7, 21–23], are the complexing agents of a specific type, the linear analogs of crown ethers, exhibiting the properties of ionophores in liquid ion-selective electrodes and the membrane carriers for various substrates.

The trend in the change of basicity of diphosphoryldiamines **XVII–XXII** as a result of introduction of phosphoryl group obeys the general laws: the change in pK_a^C occurs within the same range as in the case of monophosphorylamines (Table 7). A decrease in the difference of the dissociation constants of the first and second stages in going from 1,4-diaminobutane to 1,6-diaminohexane and their phosphorylated

Table 4. Difference in the basicity of aminophosphine oxides with primary nitrogen atom and the precursor amines

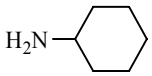
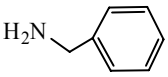
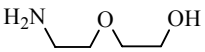
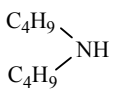
Amine	Aminophosphine oxide	ΔpK_a^C
$H_2N–C_4H_9$	**I**	9.74 – 5.61 = 4.13
XXIII	**II**	9.74 – 5.65 = 4.09
$H_2N–C_8H_{17}$	**III**	9.49 – 5.24 = 4.25
XXV	**IV**	
	**VII**	9.55 – 5.52 = 4.03
	VIII	9.55 – 5.56 = 3.99
XXVI		
	**IX**	8.42 – 4.39 = 4.03
	X	
XXX		
	**XII**	9.00 – 5.18 = 3.82
XXVII		
	**XIII**	8.85 – 5.09 = 3.76
XXVIII		
	**V**	9.60 – 4.47 = 5.13
	VI	9.60 – 4.34 = 5.26
XXXII		

Table 5. Difference in the basicity of aminophosphine oxides containing secondary and tertiary nitrogen atoms

Compound	pK_a^C
III	5.24
V	4.47
ΔpK_a^C	0.77
XII	5.18
XIV	3.90
ΔpK_a^C	1.28

derivatives can be ascribed to the weakening of the mutual influence of the amino groups with increasing distance between them.

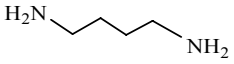
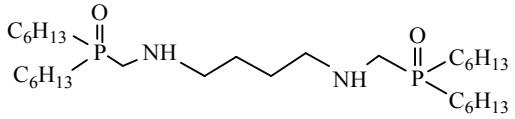
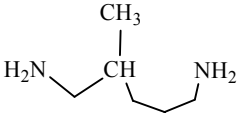
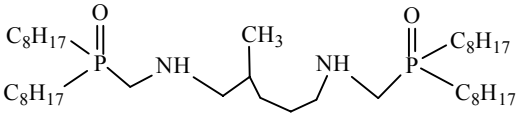
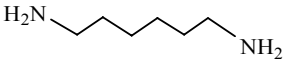
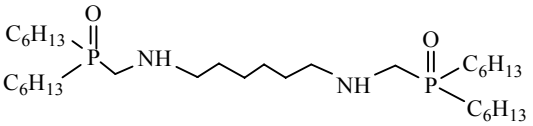
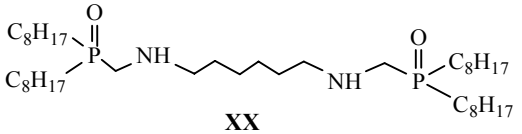
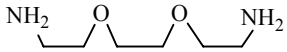
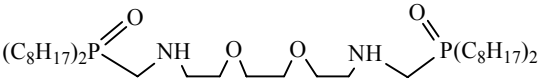
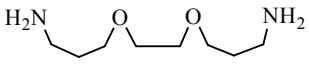
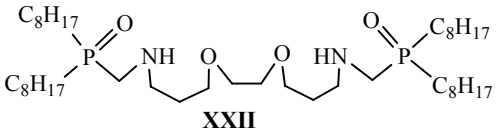
Since we have identified the pK_a^C values for a wide range of aminophosphoryl compounds in water–2-propanol medium, in the present study we regarded as necessary expressing the influence of the nature of the medium on the dissociation constants in the form of regression equations. As known, there are linear correlations between the ionization constants of the similar in structure substances in various environments, and revealing these correlations allows the prediction of the ionization constants of amines and aminophosphoryl compounds in mixed solvents. However, this approach is correct only when the principle of linearity of free energies of interaction with the environment of the participants of the acid–base equilibrium is fulfilled.

Earlier [16] we have carried out a structural and thermodynamic analysis of α-aminophosphonates acidity by estimating the Gibbs transfer energies of the participants of protolytic equilibria. We succeeded in finding that within the used reaction series these compounds interact similarly with each of the water–2-propanol solvents differing in the composition (100, 50, and 25 vol % of water). This provides the existence of linear correlations of the acidity indices for different environments and allows predicting the acid–base properties of compounds of the studied classes with diverse structure in the water–2-propanol media with different water content.

Using the same approach we determined the ionization constants of substances in the environment with a water content of 50 vol %. The aminophosphoryl compounds with long-chain hydrocarbon substituents are characterized by a very low solubility in water that makes difficult their titration in an aqueous medium. The nonphosphorylated amines, in contrast, mostly are soluble in water, so they were chosen to determine the nature of the changes in the acid–base properties in a medium containing 50 and 100% of water. Table 7 shows the experimentally obtained values of dissociation constants and the pK_a^C in water and the values found in the literature for these compounds [24]. In the calculation of the correlation parameters we also used the constants of the aminophosphoryl compounds **XLI, XLII** and **XLIV–XLVII** containing short hydrocarbon groups which make the molecules of aminophosphoryl compounds more hydrophilic.

It is known [18, 25] that such thermodynamic parameters as the changes in the Gibbs free energy (ΔG), entropy, and equilibrium constant depend on the method of expressing concentration. The use of molar and molal concentration scales leads to the fact that these values include the so-called packing term $\Delta nRT\ln 1\,000\rho_s/\overline{M}_s$, where Δn is the algebraic sum of stoichiometric coefficients, ρ_s is density, and $\overline{M}_s$ is the average molar mass of the solvent, which characterizes

Table 6. Difference in the basicity of biphosporylated diamines and parent diamines

Diamine	Phosphorylated diamine	ΔpK_a^C
 **XXXIV**	 **XVII**	
pK_{a1} 8.28	pK_{a1} 4.04	4.24
pK_{a2} 9.85	pK_{a2} 5.61	4.24
 **XXXV**	 **XVIII**	
pK_{a1} 8.85	pK_{a1} 4.93	3.92
pK_{a2} 9.74	pK_{a2} 5.25	4.49
 **XXXVI**	 **XIX**	
pK_{a1} 9.08		
pK_{a2} 10.06		
	pK_{a1} 5.38	3.70
	pK_{a2} 5.70	4.36
	 **XX**	
	pK_{a1} 5.42	3.66
	pK_{a2} 5.90	4.16
 **XXXVII**	 **XXI**	
pK_{a1} 8.20	pK_{a1} 4.30	3.90
pK_{a2} 8.98	pK_{a2} 5.25	3.73
 **XXXVIII**	 **XXII**	
pK_{a1} 8.28	pK_{a1} 5.17	3.11
pK_{a2} 9.12	pK_{a2} 5.79	3.33

the property of the solvent rather than the process in it. Thus, the interpretation of the characteristics of the equilibria occurring in the binary solvents at varying their composition can be carried out correctly using only the molar fraction scale of concentrations, which eliminates the packing term. In this regard, we discuss further only the unitary equilibrium constants calculated according to Eq. (1):

$$pK_a^N = pK_a^C + \log [c(H_2O) + c(i\text{-PrOH})], \quad (1)$$

where pK_a^N and pK_a^C are acid dissociation constants expressed in the unitary (molar-fraction) and the molar concentration scales, respectively, $c(H_2O)$ and $c(i\text{-PrOH})$ are the molar concentrations of the solvent in a binary aqueous-organic medium.

On the basis of structural-thermodynamic approach discussed in detail for similar systems in [17], we determined the values of $[\Delta_{tr}G^0(HA^+)–\Delta_{tr}G^0(A)]$, where $\Delta_{tr}G^0(HA^+)$ and $\Delta_{tr}G^0(A)$ are the Gibbs energies of transfer of the respective forms from water in 50% aqueous 2-propanol, reflecting the contributions of specific and universal solvation.

From the data listed in Table 7 it follows that replacement the Solv(w100) by Solv(w50) (the symbols in parentheses indicate the corresponding percentage by volume of water in the water–2-propanol mixtures) the protonated form of aminophosphoryl compound becomes a bit more stable than the neutral form ($[\Delta_{tr}G^0(HA^+)–\Delta_{tr}G^0(A)] < 0$). The closeness of the $([\Delta_{tr}G^0(HA^+)–\Delta_{tr}G^0(A)]$ values for the aminophosphoryl compounds and amines of different structures indicates the similarity of both specific and universal solvation in a given series of compounds.

Note that only the use of unitary constants allows the thermodynamically correct comparison of the equilibrium constants obtained in all solvents, including binary. In this case the recalculation of $pK_{a\,(w100)}^C$ in $pK_{a\,(w100)}^N$ and $pK_{a\,(w50)}^C$ in $pK_{a\,(w50)}^N$ can be carried out with Eqs. (2) and (3).

$$pK_{a\,(w100)}^N = pK_{a\,(w100)}^C + \log c(H_2O) = pK_{a\,(w100)}^C + 1.74, \quad (2)$$

$$pK_{a\,(w50)}^N = pK_{a\,(w50)}^C + \log [c(H_2O) + c(i\text{-PrOH})] = pK_{a\,(w50)}^C + 1.54. \quad (3)$$

It seemed appropriate to test whether the pK_a^N values of hydrophilic aminophosphoryl compounds correspond to the general change in the acid–base properties of the studied series of compounds. Note that at the selection of the substances for comparison of the pK_a^N no preference was done in terms of the structural features of molecules. All the pK_a^N data of the aminophosphoryl compounds and amines were used, which we could obtain owing to their solubility in these solvents.

Figure 1 shows a plot of the $pK_{a\,(w50)}^N$ of investigated substances in the medium with 50 vol % water content versus the $pK_{a\,(w100)}^N$ values in water. The dependence is linear with a good correlation coefficient. After the linearization by the least-squares method we obtained a correlation equation reflecting the influence of environment on the basicity of the studied aminophosphoryl compounds and the original amines.

$$pK_{a\,(w50)}^N = (0.921 \pm 0.023)\, pK_{a\,(w50)}^N – (0.110 \pm 0.224),$$
$$R = 0.9857,\ N = 22.$$

For the quantitative description of the effect of phosphorylation on the basicity of the amino compounds in the framework of the principle of linear free energy relationship we constructed a plot showing the relationship between dissociation constants of the compounds and similar constants of their nonphosphorylated counterparts, the simple amines (Fig. 2).

Table 7. Ionization constants (pK_a^C and pK_a^N) of the aminophosphoryl compounds and amines at 298±0.2 K

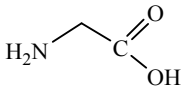
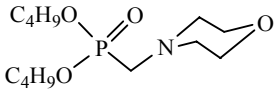
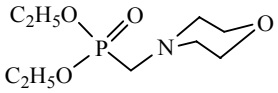
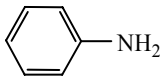
Comp. no.	Formula	$pK_{a\,(w50)}^C$ ±0.05	$pK_{a\,(w50)}^N$ ±0.05	$pK_{a\,(w100)}^C$ ±0.05	$pK_{a\,(w100)}^N$ ±0.05	$\Delta_{tr}G^0_{w100\to w50}(HA^+) – \Delta_{tr}G^0_{w100\to w50}(A)$, ±0.6 kJ mol^{-1}
XXXIX	$H_3PO_4 \cdot 12H_2O$	2.65	4.19	2.12	3.86	–10.5
		7.01	8.55	7.2	8.94	–6.4
XL		2.33	3.87	2.34	4.08	–7.4
XLI		3.00	4.54	3.62	5.36	–3.9
XLII		3.30	4.84	3.90	5.64	–4.0
XLIII		3.99	5.53	4.58	6.32	–4.1

Table 7. (Contd.)

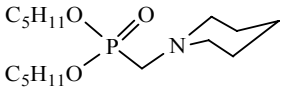
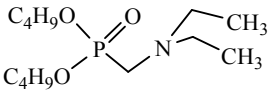
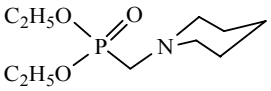
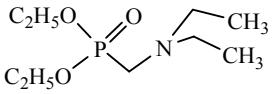
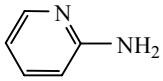
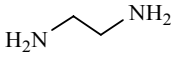
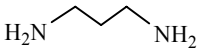
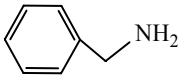
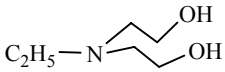
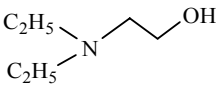
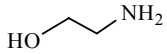
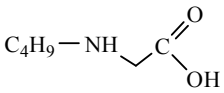
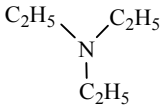
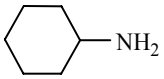
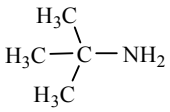
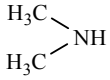
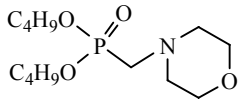
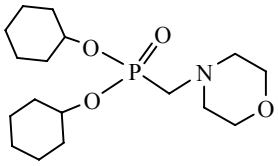
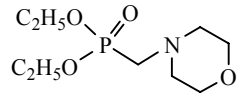
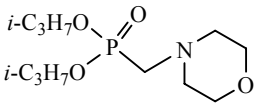
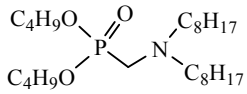
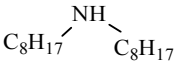
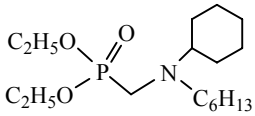
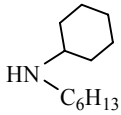
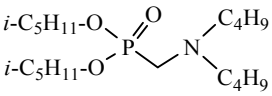
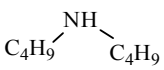
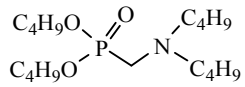
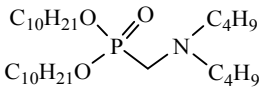
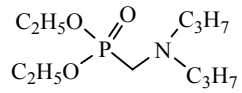
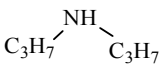
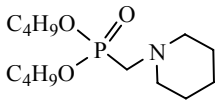
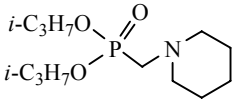
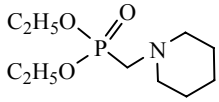
Comp. no.	Formula	$pK_{a\,(w50)}^{C}$ ±0.05	$pK_{a\,(w50)}^{N}$ ±0.05	$pK_{a\,(w100)}^{C}$ ±0.05	$pK_{a\,(w100)}^{N}$ ±0.05	$\Delta_{tr}G^{0}_{w100\to w50}(HA^{+}) - \Delta_{tr}G^{0}_{w100\to w50}(A)$, ±0.6 kJ mol^{-1}
XLIV		5.19	6.73	5.98	7.72	–3.0
XLV		5.46	7.00	6.48	8.22	–1.6
XLVI		5.73	7.27	6.54	8.28	–2.8
XLVII		5.80	7.34	6.60	8.34	–2.9
XLVIII		6.19	7.73	6.96	8.70	–3.1
XLIX		6.63 9.33	8.17 10.87	6.99 10.08	8.73 11.82	–5.4 –3.2
L		9.83 7.97	11.37 9.51	10.51 8.48	12.25 10.22	–3.6 –4.6
LI		8.42	9.96	9.25	10.99	–2.7
LII		8.46	10.00	9.12	10.86	–3.7
LIII		8.93	10.47	9.98	11.72	–1.5
LIV		9.00	10.54	9.50	11.24	–4.6
LV		9.37	10.91	10.07	11.81	–3.5
LVI		9.58	11.12	10.87	12.61	–0.1
LVII		9.68	11.22	10.66	12.40	–1.9
LVIII	C_4H_9–NH_2	9.74	11.28	10.78	12.52	–1.5
LIX		9.99	11.53	10.45	12.19	–4.8
LX		10.04	11.58	10.93	12.67	–2.4

Table 8. Ionization constants (pK_a^C and pK_a^N) of the amines and α-aminophosphonates at 298±0.2 K

Comp. no.	Formula	$pK_{a\,(w100)}^{C}$ ±0.05	$pK_{a\,(w100)}^{N(AP)}$ ±0.05	Amine	$pK_{a\,(w100)}^{C}$ ±0.05	$pK_{a\,(w100)}^{N(AP)}$ ±0.05
LXI		3.00	4.74		8.11	9.85
LXII		3.11	4.85			
LXIII		3.3	5.04			
LXIV		3.37	5.11			
LXV		3.67	5.41		8.98	10.72
LXVI		4.52	6.26		9.52	11.26
LXVII		4.23	5.97		9.6	11.34
LXVIII		4.34	6.08			
LXIX		4.63	6.37			
LXX		4.99	6.73		9.89	11.63
LXXI		5.37	7.11		10.98	12.72
LXXII		5.67	7.41			
LXXIII		5.73	7.47			

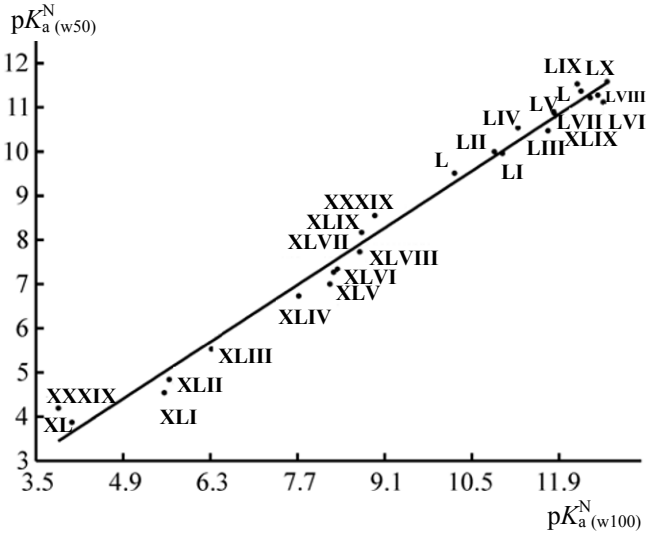


Fig. 1. The relationship between the unitary dissociation constants of aminophosphoryl compounds and amines in water and water–2-propanol mixture containing 50% water, μ = 0.05, 298 ± 0.2 K.

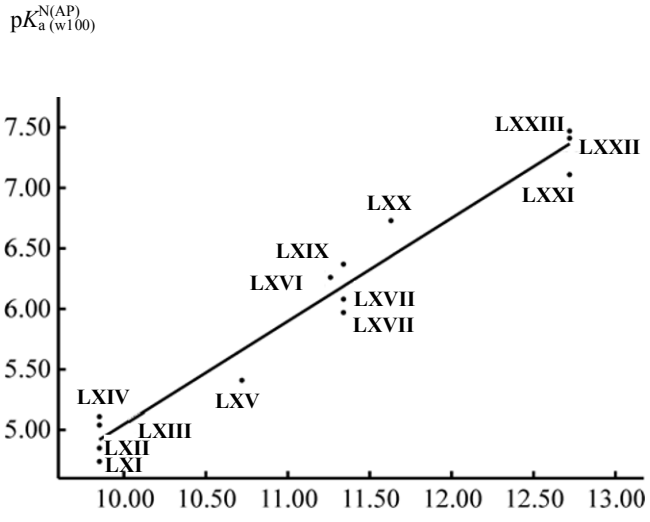


Fig. 2. The relationship between the unitary dissociation constants of some aminophosphoryl compounds and precursor amines, μ = 0.05, 298 ± 0.2 K.

After the linearization by the least-squares method we obtained a correlation equation reflecting the influence of environment on the basicity of the studied aminophosphoryl compounds and the source amines:

$$pK_a^{P=O} = (0.852 \pm 0.051)pK_a^{A} - (3.4673 \pm 0.577),$$

$$R = 0.9579;\ N = 13.$$

The above regression equations indicate, on the one hand, that the solvation of the investigated compounds in the media used is of the same type and, on the another hand, they allow us to predict successfully the acid–base properties of these compounds with varied structures and in the media differing by the water content.

EXPERIMENTAL

Potentiometric titration of aminophosphoryl compounds and amines was carried out using a glass electrode ES-1060, a silver chloride reference electrode ESR-1010, a universal ionomer I-160MI-6, and a thermostat U15 MLW. Solutions were prepared using 2-propanol of chemically pure grade, potassium chloride of high purity grade, and twice distilled water.

For the potentiometric titration precisely weighted samples of aminophosphoryl compounds (0.3–0.5 mmol) were prepared. A sample was dissolved in 20 ml of the supporting electrolyte consisting of 0.05 N solution of potassium chloride in a 2-propanol–water mixture containing 50 vol % of water. The resulting solution was placed in a 30 ml electrochemical cell equipped with a mechanical stirrer with an electric drive and a microburette (scale 0.02 ml, volume 5 ml), the cell content was titrated with a 0.05 M solution of HCl in aqueous 2-propanol. The indicator electrode potential was measured with 2–3 min delay after adding the next portion of the titrant. The change in the hydrogen ion concentration during the titration was recorded by measuring the potential of glass electrode with respect to silver chloride. Before measuring, the electrodes were kept in 0.1 N aqueous solution of HCl in 2-propanol for several days. Calibration of glass electrode was performed as described in [9].

The obtained analytical data on the dependence of potential on the amount of added titrant were processed on a computer using the original software created with the Visual Basic. The algorithm includes the Gran linearization of the titration curve. Titration curves of dibasic aminophosphoryl compounds were processed using the CPESSP similar to [16].

Synthesis of α-aminophosphoryl compounds was carried out by the Kabachnik–Fields reaction in the ternary system of hydrophosphoryl compound–paraformaldehyde–amine. The methods of the synthesis and characteristics of the compounds **I–VIII, XIV, XVI, XX** are given in [4, 6, 12, 16].

The NMR spectra of compounds were recorded on a Varian XL 300 instrument at the operating frequency 122.4 MHz for ^{31}P nuclei (external reference 85% phosphoric acid) and 300 MHz for ^{1}H nuclei (solvent

$CDCl_3$, external TMS). The IR spectra were recorded on a Fourier transform infrared spectrometer Tenson 27 (Bruker). The melting points were determined on a Stuart melting point device SMP3 or by TG and DSC analysis on a NETZSCH STA 449C instrument. The R_f values were determined by thin layer chromatography on silica gel (Silufol UV 254), the mobile phase was acetone–chloroform–methanol mixture 5:8:1 (by volume), the developer was iodine vapor and then distilled water.

The compounds described below were obtained by the general method described in [4].

***N*-Benzylmethylenedihexylphosphine oxide (IX).** Yield 90 %, mp 56.3°C, R_f 0.53. IR spectrum, ν, cm^{-1}: 1151 (P=O), 1456 and 1469 (Ph), 3279 (N–H) (vaseline oil). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.88 two t (6H, CH_3, Hex, $^3J_{HH}$ 6.77), 1.27–1.76 m (20H, P[(C<u>H</u>$_2$)$_5$C<u>H</u>$_3$]$_2$), 2.84 d (2H, PC<u>H</u>$_2$N, $^2J_{PH}$ 8.09), 3.85 s (2H, NC<u>H</u>$_2$Ph), 7.33–7.24 m (5H, NCH$_2$C$_6$<u>H</u>$_5$). ^{31}P NMR spectrum (toluene): δ_P 44 ppm. Found, *m*/*e*: 337.8. $C_{20}H_{36}NOP$. Calculated, *m*/*e*: 337.5.

***N*-Benzylmethylenedioctylphosphine oxide (X).** Yield 94 %, mp 49.8°C, R_f 0.57. IR spectrum, ν, cm^{-1}: 1151 (P=O), 1458, 1467 (Ph), 3272 (N–H) (vaseline oil). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.88 two t, (6H, CH_3, Oct, $^3J_{HH}$ 6.72), 1.26–1.76 m (28H, P[(C<u>H</u>$_2$)$_7$C<u>H</u>$_3$]$_2$), 2.84 d (2H, PC<u>H</u>$_2$N, $^2J_{PH}$ 8.08), 3.85 s (2H, NC<u>H</u>$_2$Ph), 7.36–7.31 m (5H, NCH$_2$C$_6$<u>H</u>$_5$). ^{31}P NMR spectrum (toluene): δ_P 43 ppm. Found, *m*/*e*: 394.1. $C_{24}H_{44}NOP$. Calculated, *m*/*e*: 393.6

Dihexyl-β-(2-pyridyl)aminophosphine oxide (XI). Yield 70%, n_D^{20} 1.5119, R_f 0.42. ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.85 two t (6H, CH_3, Hex, $^3J_{HH}$ 6.79), 1.17–1.77 m (20H, P[(C<u>H</u>$_2$)$_5$C<u>H</u>$_3$]$_2$), 3.86 d (2H, PC<u>H</u>$_2$N, $^2J_{PH}$ 2.26), 4.76 br.s (1H, NH), 6.38–6.49 m [NCCHCHC<u>H</u> (ring)], 6.51–6.59 m [NCC<u>H</u> (ring)], 7.30–7.40 m [NCCHCHCHC<u>H</u> (ring)], 7.97–8.06 m [NCCHC<u>H</u> (ring)] ($CDCl_3$). ^{31}P NMR spectrum (1,4-dioxane): δ_P 54 ppm.

***N*-(Didecylphosphoryl) methyl ethanolamine (XII).** Yield 89%, mp 40.0°C, R_f 0.24. IR spectrum, ν, cm^{-1}: 1143 (P=O), 3051 – 3700 (N–H, O–H) (vaseline oil). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.91 two t (6H, CH_3, Dec, $^3J_{HH}$ 6.63), 1.18–1.90 m (36H, P[(C<u>H</u>$_2$)$_9$C<u>H</u>$_3$]$_2$), 2.26 br.s (1H, OH), 2.91–2.97 m (2H, NC<u>H</u>$_2$CH$_2$), 3.01 d (2H, PC<u>H</u>$_2$N, $^2J_{PH}$ 6.99), 3.70–3.73 t (2H, CH$_2$C<u>H</u>$_2$O, $^3J_{HH}$ 4.8). ^{31}P NMR spectrum (toluene): δ_P 43 ppm.

***N*-[(Dioctylphosphoryl)methyl]-2-(2-aminoethoxy)-ethanol (XIII).** Yield 73%, n_D^{20} 1.4771, R_f 0.28. IR spectrum, ν, cm^{-1}: 1138 (P=O), 3076 – 3654 (N–H, O–H) (thin film). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.85 two t (6H, CH_3, Oct, $^3J_{HH}$ 6.66), 1.16–1.80 m [28H, P(C<u>H</u>$_2$)$_7$CH$_3$)$_2$], 2.62 br.s (1H, OH), 2.85 m (2H, NC<u>H</u>$_2$CH$_2$, $^3J_{HH}$ 5.10), 2.90 d (2H, PCH$_2$N, $^2J_{PH}$ 7.78), 3.60–3.53 t (4H, CH$_2$OCH$_2$), 3.70–3.67 t (2H, C<u>H</u>$_2$OH). ^{31}P NMR spectrum (benzene): δ_P 48 ppm. Found, %: P 7.23; $C_{21}H_{41}NO_3P$. Calculated, %: P 6.92.

***N*-[(Dihexylphosphoryl)methyl]-*N*-[(didecylphosphoryl)methyl]octylamine (XV)** Yield 70%, oil, R_f 0.45. IR spectrum, ν, cm^{-1}: 1164 (P=O) (thin film). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.80–0.90 t (15H, CH_3, Hex, Oct, and Dec), 1.14–1.84 m (68H, P[(C<u>H</u>$_2$)$_5$CH$_3$]$_2$, NCH$_2$(C<u>H</u>$_2$)$_6$CH$_3$, P[(C<u>H</u>$_2$)$_9$CH$_3$]$_2$), 2.76–2.84 t (2H, NC<u>H</u>$_2$CH$_2$, Oct), 2.89 d (4H, [PCH$_2$N]$_2$, $^2J_{PH}$ 5.61). ^{31}P NMR spectrum (toluene): δ_P 44 ppm.

***N*,*N*'-Bis(dihexylphosphorylmethyl)-1,4-diaminobutane (XVII).** Yield 85%, mp 64.0°C, R_f 0.11. IR spectrum, ν, cm^{-1}: 1150 (P=O), 3280 (N–H) (vaseline oil). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.86 t (12H, C<u>H</u>$_3$, Hex, $^3J_{HH}$ 6.60), 1.15–1.85 m {44H, NHCH$_2$(C<u>H</u>$_2$)$_2$CH$_2$NH, P[(C<u>H</u>$_2$)$_5$CH$_3$]$_2$}, 2.77 t (4H, NC<u>H</u>$_2$CH$_2$, $^3J_{HH}$ 6.00), 2.98 d (4H, PCH$_2$N, $^2J_{PH}$ 7.20). ^{31}P NMR spectrum (benzene): δ_P 48 ppm. Found, %: C 64.99; H 12.33; N 4.95. $C_{30}H_{66}N_2O_2P_2$. Calculated, %: C 65.66; H 12.12; N 5.10.

***N*,*N*'-Bis(dioctylphosphorylmethyl)-2-methyl-1,5-diaminopentane (XVIII).** Yield 90%, mp 60.0°C, R_f 0.25. IR spectrum, ν, cm^{-1}: 1150 (P=O), 3285 (N–H) (vaseline oil). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.91 t (8H, C<u>H</u>$_3$, Oct, $^3J_{HH}$ 6.90), 0.93 t (3H, CHC<u>H</u>$_3$, $^3J_{HH}$ 6.30), 1.20–1.85 m (60H, CH(C<u>H</u>$_2$)$_2$CH$_2$NH, P[(C<u>H</u>$_2$)$_7$CH$_3$]$_2$), 2.59 d.d (1H, NC<u>H</u>^{A}H^{B}CH, $^2J_{HH}$ 11.40, $^3J_{HH}$ 6.00), 2.45 d.d (1H, NCH^A<u>H</u>^{B}CH, $^2J_{HH}$ 11.40, $^3J_{HH}$ 6.00), 2.91 d (2H, PCH$_2$N, $^2J_{PH}$ 7.20), 2.89 d (2H, PCH$_2$N, $^2J_{PH}$ 7.50). ^{31}P NMR spectrum (chloroform): δ_P 48 ppm.

***N*,*N*'-Bis(dihexylphosphorylmethyl)-1,6-diaminohexane (XIX).** Yield 85%, mp 68.0°C, R_f 0.13. IR spectrum, ν, cm^{-1}: 1149 (P=O), 3287 (N–H) (vaseline oil). ^1H NMR spectrum, δ, ppm, *J*, Hz: 0.86 t (8H, C<u>H</u>$_3$, Hex, $^3J_{HH}$ 6.90), 1.15–1.85 m {48H, NHCH$_2$·(C<u>H</u>$_2$)$_4$CH$_2$NH, P[(C<u>H</u>$_2$)$_5$CH$_3$]$_2$}, 2.60 t (4H, NC<u>H</u>$_2$CH$_2$, $^3J_{HH}$ 6.90), 2.84 d (4H, PCH$_2$N, $^2J_{PH}$ 7.80), ($CDCl_3$). ^{31}P NMR spectrum (toluene): δ_P 43 ppm. Found, %: C 66.63; H 8.76; N 4.86. $C_{32}H_{70}N_2O_2P_2$. Calculated, %: C 67.05; H 9.01; N 4.81.

***N,N'*-Bis(dioctylphosphorylmethyl)-1,8-diamino-3,6-dioxaoctane (XXI).** Yield 69%, mp 45.0°C, R_f 0.08. IR spectrum, ν, cm^{-1}: 1150 (P=O), 3180 (N–H), 1110 (C–O–C) (vaseline oil). ^{1}H NMR spectrum, δ, ppm, *J*, Hz: 0.91 t (12H, C$\underline{H}_3$, Oct, $^3J_{HH}$ 6.60), 1.15–1.85 m {56H, P[(C$\underline{H}_2$)$_7$CH$_3$]$_2$}, 2.91 t (4H, NC$\underline{H}_2$CH$_2$, $^3J_{HH}$ 4.90), 2.98 d (4H, PCH$_2$N, $^2J_{PH}$ 7.80), 3.63 t (4H, OC$\underline{H}_2$CH$_2$N, $^3J_{HH}$ 6.00), 3.63 s (4H, OCH$_2$CH$_2$O). ^{31}P NMR spectrum (chloroform): δ_P 49 ppm.

***N,N'*-Bis(dioctylphosphorylmethyl)-1,10-diamino-4,7-dioxadecane (XXII).** Yield 79%, mp 55.0°C, R_f 0.10. IR spectrum, ν, cm^{-1}: 1150 (P=O), 3180 (N–H), 1110 (C–O–C) (vaseline oil). ^{1}H NMR spectrum, δ, ppm, *J*, Hz: 0.92 t (12H, C$\underline{H}_3$, Oct, $^3J_{HH}$ 6.90), 1.15–1.85 m {60H, NHCH$_2$C$\underline{H}_2$CH$_2$O, P[(C$\underline{H}_2$)$_7$CH$_3$]$_2$}, 2.78 t (4H, NC$\underline{H}_2$CH$_2$, $^3J_{HH}$ 7.80), 2.92 d (4H, PCH$_2$N, $^2J_{PH}$ 7.80), 3.56 t (4H, OC$\underline{H}_2$CH$_2$CH$_2$, $^3J_{HH}$ 6.45), 3.59 s (4H, OCH$_2$CH$_2$O). ^{31}P NMR spectrum (benzene): δ_P 44 ppm.

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