# Synthesis of the novel β-aminophosphoryl compounds and their acid-base properties and membrane-transport abilities towards carboxylic acids

*R. A. Cherkasov,[a]* A. R. Garifzyanov,[a] N. V. Kurnosova,[a] E. V. Matveeva,[b] and I. L. Odinets[b]**

[a]*Kazan (Volga Region) Federal University,*
*18 ul. Kremlevskaya, 420008 Kazan, Russian Federation.*
*E-mail: rafael.cherkasov@ksu.ru*
[b]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,*
*28 ul. Vavilova, 119991 Moscow, Russian Federation.*
*E-mail: odinets@ineos.ac.ru*

The highly efficient synthesis of β-aminophosphoryl compounds with one and two ethylphosphoryl groups was performed by the addition of amines to the vinylphosphoryl compounds in water as a solvent. The acid-base properties and membrane-transport abilities of the target compounds towards carboxylic acids were studied. Selectivity towards acetic acid was revealed.

**Key words:** β-aminophosphonates, β-aminophosphine oxides, green chemistry, reactions in water, acid-base properties, membrane-transport properties, carboxylic acids.

Pronounced interest appeared in recent decades in the development of synthesis methods and investigation of the properties of ω-aminophosphoryl compounds is caused by a wide scope of practically useful compounds of this type. Being analogs of natural amino acids, they possess diverse biological activity, the type of which is determined by both the linker length and the environment of the nitrogen and phosphorus atoms, and serve as objects of intensive studies of both synthetic chemists and specialists in the areas of biochemistry, pharmaceutics, medicine, agriculture, and other related disciplines.[1—3]

The corresponding α-aminophosphonates and their derivatives, among which the substances were revealed that exhibit antibacterial, antiviral, and antifungal activities and properties of inhibitors of metalloproteases, growth factors, *etc.*,[3] have been studied in most detail to the present time. The aminophosphoryl framework of these molecules combines the phosphoryl and amine functional groups, which are responsible for the manifestation of complexation properties predetermining the possibility of their use as liquid and membrane extracting agents for objects of various nature: organic and inorganic acids and alkaline, alkaline-earth, rare, scattered, and noble metals.[4—7]

At the same time, the study of the properties of the β-aminophosphoryl compounds related in structure has not attracted considerable attention up to presently, although a series of similar compounds also exhibit a broad spectrum of biological activity[8] and their complexation ability towards a wide series of metal ions forms a basis for their possible use for the development of selective ionophores and membrane carriers.[9]

In the present work, we synthesized novel β-aminophosphoryl compounds with one (**1**—**5**) and two (**6** and **7**) β-ethylphosphoryl groups containing the secondary or tertiary nitrogen atom in order to study the acid-base properties and membrane-transport abilities of the β-aminophosphoryl compounds towards acidic substrates, *viz.*, carboxylic acids with different structures (monobasic acetic and dibasic oxalic and tartaric acids containing several proton-donor groups), which could predetermine variety of possibilities of their binding with carrier molecules. Their α-analogs were also used for comparison: phosphine oxide (**8**) and phosphonate (**9**) containing the highly lipophilic *n*-octyl groups at potential coordination sites (nitrogen and phosphorus atoms).

The optimum in terms of simplicity method for the synthesis of β-aminophosphonates is the addition of amines to the terminal bond of vinyl phosphonates,[10—12] which is usually carried out under rather drastic conditions (prolong heating in the presence of amine excess, the use of the basic catalysts, *etc.*). We have recently shown[13—15] that the use of water as a solvent (in the absence of any organic cosolvent or catalyst) substantially increases the rate of this reaction, giving the target products in yields close to quantitative. Both water-soluble (diethyl vinylphosphonate)[13] and insoluble in water (diphenylvinylphosphine oxide)[14,15] organophosphorus substrates can be used in the reaction, and the decrease in the reaction rate can be compensated by an elevated temperature (100 °C),

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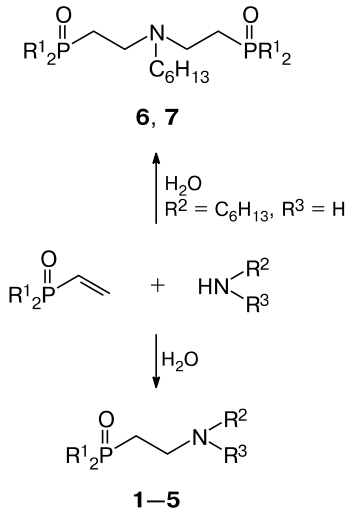
which does not result in any secondary interactions. Unlike the classical conditions of this reaction, the use of water corresponding to all principles of green chemistry makes it possible to perform easily the double phosphonoethylation of primary amines to form bis(β-ethylphosphoryl)amines when using stoichiometric ratios of the reactants.

Therefore, the novel β-aminophosphoryl compounds were synthesized in water as a solvent. Although the reaction rate for dibutyl vinylphosphonate is somewhat lower than that for its analog with the ethoxy groups at the phosphorus atom,[13] the addition of hexylamine and octylamine (compounds **2** and **3**) proceeds smoothly at ambient temperature (Scheme 1). At the same time, it is reasonable to perform the reaction on heating at a decrease in the solubility of one of the reactants, for example, when dioctylamine (compounds **4** and **5**) or diphenylvinylphosphine oxide (compounds **1** and **5**) is used and when double phosphonoethylation (compounds **6** and **7**) is carried out. In most cases, the products were isolated by lyophilic drying, whereas additional purification by flash chromatography was required for compounds **4** and **7**.

**Scheme 1**




$R^1$ = Ph, $R^2$ = $C_6H_{13}$, $R^3$ = H (**1**); $R^1$ = OBu, $R^2$ = $C_6H_{13}$, $R^3$ = H (**2**); $R^2$ = $C_8H_{17}$, $R^3$ = H (**3**); $R^2$ = $R^3$ = $C_8H_{17}$ (**4**); $R^1$ = Ph, $R^2$ = $R^3$ = $C_8H_{17}$ (**5**); $R^1$ = OBu (**6**), OEt (**7**)

The compositions and structures of the synthesized compounds were confirmed by the elemental analysis, IR spectroscopy, and multinuclear NMR spectroscopy data. According to the elemental analysis data, compound **5** is a stable hemihydrate. The IR spectra of β-aminophosphoryl compounds **1**—**7** contain the characteristic absorption bands of the phosphoryl group at 1237—1248 and 1180—1184 $cm^{-1}$ for phosphonates and phosphine oxide, respectively. The $^{31}P$ NMR spectra exhibit singlet signals with δ ~31 characteristic of this type of environment of the phosphorus atom. The $^1H$ and $^{13}C$ NMR spectra completely correspond to the structure of the synthesized compounds and contain the signals of the protons and carbons of the $PCH_2$ and $NCH_2$ groups, respectively, in addition to the characteristic groups of signals of the corresponding substituents at the phosphorus and nitrogen atoms.

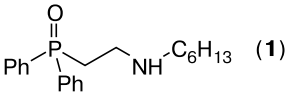
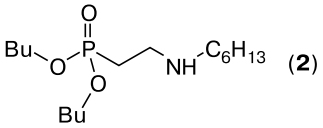
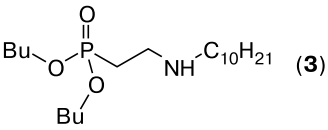
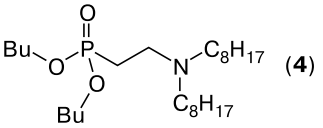
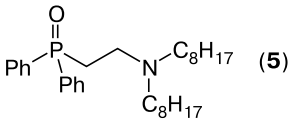
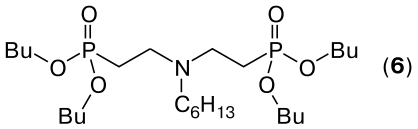
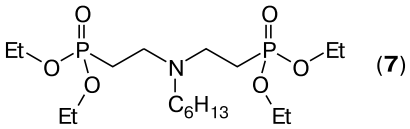
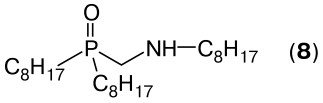
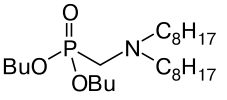
When estimating the efficiency of membrane transport of proton substrates, important information can be obtained by comparing the values of transfer flows and acid-base properties of carrier molecules. For a large array of the α-aminophosphoryl compounds, we determined the acidic dissociation rate constants of the conjugated acids in a medium of aqueous propan-2-ol[16—19] and, for a few number of examples, respective constants of their β-aminophosphoryl analogs were determined.[11] A comparison of the obtained values of p$K_a$ with the corresponding values for the amine-precursors showed that β-phosphorylamines exceed in basicity the α-derivatives with similar structure by 2—3 p$K_a$ units, on the average, and are inferior by 4—5 p$K_a$ units to the corresponding amines. A similar decrease in basicity was explained by a strong acceptor influence of the phosphoryl group situated through two or one carbon atom, respectively, from the basic site, nitrogen atom.

The p$K_a$ values of the aminophosphoryl compounds used in this work were determined by potentiometric titration according to a described procedure[20]; their values are given in Table 1.

As can be seen from the data in Table 1, the earlier observed regularities of changing the p$K_a$ values of the conjugated acids, their dependence on the distance between the phosphoryl group and the proton-acceptor site (nitrogen atom) are manifested in this experiment: the basicity of β-phosphorylamines **1**—**3** is almost independent of the nature of substituents at the phosphorus atom and exceeds the same value for the α-analogs by 2—4 p$K_a$ units. A fairly sharp decrease in the basicity of diphosphorylated amines **6** and **7** also fits well with the general tendency: the introduction of the second acceptor phosphoryl group more strongly decreases the electron density on the nitrogen atom. Note that the decrease in the basicity in α,α-bis(dialkylphosphorylmethyl)amines is so high that their values are below the limits of experimental determination (p$K_a$ < 2).[18] Naturally, two dialkoxyphosphoryl groups arranged by one methylene fragment farther from the nitrogen atom (**6** and **7**) exert a smaller electron-acceptor effect on the basic site, decreasing, nevertheless, the values of p$K_a$ by 2—3 units compared to β-monophosphorylated amines.

The values of p$K_a$ of preceding amine determined by us under the same conditions as the acidic dissociation of phosphorylamines (water—propan-2-ol (1 : 1), 25 °C), were 9.49, 8.98, and 9.68 for octylamine, dioctylamine, and hexylamine, respectively; *i.e.*, the difference in basic-

**Table 1.** Characterization of the acid-base and membrane-transport properties of the aminophosphoryl compounds

| Aminophosphoryl compound | p$K_a$[a] | Transfer flow,[b] $T \cdot 10^6$/mol m$^{-2}$ min$^{-1}$ | | |
|---|---|---|---|---|
| | | Acetic acid | Oxalic acid | Tartaric acid |
|  (**1**) | 7.46 | 1.40 | 3.04 | $<10^{-7}$ |
|  (**2**) | 7.33 | 6.00 | 0.29 | $<10^{-7}$ |
|  (**3**) | 7.37 | 10.20 | 8.17 | $<10^{-7}$ |
|  (**4**) | 5.83 | 267.90 | 77.50 | 0.51 |
|  (**5**) | 6.15 | 148.6 | 104.17 | 1.83 |
|  (**6**) | 4.45 | 32.67 | 1.97 | $<10^{-7}$ |
|  (**7**) | 4.81 | —[d] | 0.25 | $<10^{-7}$ |
|  (**8**) | 5.23 | 872.00 | —[c] | $<10^{-7}$ |
|  (**9**) | 3.68 | 153.26 | 52.15 | $<10^{-7}$ |

[a] Constant for the aminophosphoryl compounds.
[b] The concentration of the carrier in the membrane phase is 0.2 mol L$^{-1}$, and the substrate concentration is 0.2 mol L$^{-1}$.
[c] Forms a complex insoluble in the membrane.
[d] Washed out of the membrane.

ity of β-phosphorylamines and their amine-precursors was 2—4 p$K_a$ units for mono- (**1—5**) and 4—5 p$K_a$ units for di-(phosphorylethyl)amines **6** and **7**. This is well consistent with the earlier revealed and above discussed regularities.

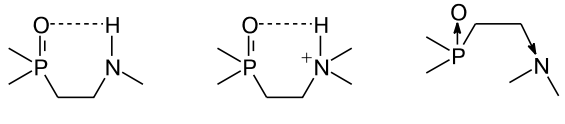
Note that the results obtained explain the possibility of occurrence of double phosphonoethylation in water, where N-nucleophiles with p$K_a$ higher than 6 easily enter the reaction. In other words, the formed products with one ethylphosphoryl group are appropriate as N-nucleophiles for the reaction under these conditions. In addition, the difference in the basic properties of the primary amines and their β-aminophosphoryl derivatives reasonably ex-

plains the reaction of double phosphonoethylation as a step-by-step process, where the β-aminophosphoryl product that formed cannot compete with the primary amine as an N-nucleophile.

The difference in the values of basicity of secondary (**1**—**3**) and tertiary (**4** and **5**) phosphorylated amines is significant and also obvious for the comparison of $pK_a$ of their α-analogs **8** and **9**. A similar phenomenon has earlier been observed[16] for many examples in the structural analogs of β-aminoethyl phosphonates studied in this work, *viz.*, α-aminoalkyl phosphonates and α-phosphine oxides. This phenomenon was explained assuming that the intramolecular H-complexes N—H···O=P are involved in the acid-base equilibria of secondary phosphorylamine molecules. It is most likely that this effect takes place in the series of their β-analogs as well. It can be assumed that the thermodynamically favorable formation of the six-membered ring predetermines the affinity of secondary β-phosphorylamines to intramolecular hydrogen bonding to complex **A**.

Indeed, the identical character of the IR spectra of compound **2**, in particular, the absorption bands of the P=O group at 1246 $cm^{-1}$ and the broad adsorption NH band at 3306 $cm^{-1}$ in thin layer and in $CCl_4$ solutions (at different dilutions) indicate that the molecule includes the intramolecular hydrogen bond with the formation of the six-membered H-ring. The absorption bands of the unbound groups, $\nu_{P=O}$ and $\nu_{NH}$, are absent from the spectra. Nevertheless, it should be mentioned that in crystal of the single structurally characterized β-aminophosphoryl compound, [2-(*tert*-butylamino)ethyl]diphenylphosphine oxide [$Bu^tNH(CH_2)_2P(O)Ph_2$], the molecules are bound by strong intermolecular hydrogen bonds P(O)...H—N($Bu^t$) involving the phosphoryl oxygen atom.[21]

Evidently, the protonated form of β-phosphorylamines is able to H-complexation by type **B**; however, the formation of this H-complex requires the conformational transition of *trans*-form **C**, in which the phosphorylamine molecules exist due to the repulsion of the strong P→O and C→N dipoles,[16] to the *cis*-conformation favorable for the formation of the six-membered ring in complex **B**. It is most likely that the energy of transformation of the neutral molecule of tertiary phosphine to the intramolecular H-complex of conjugated acid **C** affects the differences in basicity of secondary and tertiary amines. However, the role of other factors cannot be excluded, for example, hydrophobic interactions of bulky substituents or solvation of the protonation sites differed by steric characteristics.




We studied the possibility of using the newly synthesized aminophosphoryl compounds for the transfer of acidic substrates through liquid impregnated membranes. The experimental method and its mathematical processing are similar to those described earlier.[22] Phenylcyclohexane was chosen as a membrane medium, since this solvent is highly boiling and indifferent to molecules of substrates and carriers and provide stable conditions of measuring the values of transfer flows.

The literature[23] and our earlier[24] data on the mechanism of membrane transport of the proton-donor substrates by the neutral phosphoryl and amine carriers indicate in favor of the solvate mechanism, which assumes the membrane extraction of carboxylic acid by the aminophosphoryl reactants in the form of H-complexes, and it is the nitrogen atom that acts as the protonation site. It is natural to assume that the transfer of the chosen acids by the β-aminophosphoryl reactants also occurs with the preliminary formation of the H-complex of the $O=PCH_2CH_2N\cdots H—A$ type, the easiness of formation of which depends on the basicity of the amine center and the strength of the transferred acid.

However, as we indicated several times,[22,24] the attempts to reveal rather simple interrelations of the structures of the carrier and substrate, on the one hand, and the values of transfer flows (transfer efficiencies), on the other hand, are unsuccessful, as a rule. This is related to the influence of many, often mutually compensating factors on the efficiency. The value of the transfer flow depends, obviously, on the binding rate of the carrier with the substrate and on the easiness of re-extraction in the accepting phase. In addition, in polyfunctional complexing agents of the type of the aminophosphoryl compounds studied by us, not all but these or other coordination sites (for example, for steric reasons) can participate in binding with the transferred substrate. One of the important factors can be a change in the viscosity of the membrane phase with changing the concentration and nature of the transferred complex and some other hardly taken into account characteristics of the process and its participants.[25,26] However, as shown, in particular, by the results of the present study, the hydrophilic (lipophilic) characteristics of the extracting agent are among the most significant parameters determining the interfacial transfer rate; *i.e.*, we speak about such a hardly expressed characteristic as hydrophilic—lipophilic balance.

We have previously shown[16] using the correlations that only the aminophosphoryl compounds, whose molecules contain at least 20 carbon atoms, can serve as efficient liquid and membrane extracting agents. In this case, the interfacial partition coefficient in water—organic solvent systems exceeds six logarithmic units and, hence, losses of the transfer due to its retention in the aqueous phase can be avoided.

An analysis of the values of transfer flows of carboxylic acids by the aminophosphoryl carriers of different structure presented in Table 1 revealed no explicit dependence

of the basicity of the proton acceptor or strength of the acid. The most efficient membrane extracting agents of acetic and oxalic acids were those containing long-chain hydrocarbon groups at the nitrogen and phosphorus atoms. α-Aminophosphine oxide **8**, which is less basic than all β-aminophosphoryl compounds used in the work, demonstrates the highest flow value. The significance of the lipophilic properties of the carrier is also confirmed by a comparison of the transfer flow values of acids by mono- and bisphosphorylamines: less basic and more lipophilic diphosphorylamine **6** noticeably exceeds its monophosphorylated analog **2** in transfer efficiency, and the substituents at the nitrogen and phosphorus atoms are the same.

In the general case, the same aminophosphoryl groups are more active in processes of membrane transport of monobasic acetic acid than in the case of dibasic oxalic acid. The probable reason for this difference can be the nature of H-complexes formed by molecules of phosphorylamines and carboxylic acids. If assuming that they include one acid molecule and one amine molecule, the complex formed by oxalic acid contains the unbound "excessive" carboxyl group well solvated by water molecules in the donating aqueous phase. In this case, an almost complete absence of membrane transport by the chosen tartaric acid becomes clear. Evidently, an excess of hydrophilic carboxyl and hydroxyl groups in the complexes formed by tartaric acid results in their strong retention in the donating aqueous solution. A similar effect was observed earlier[22,24] when studying the membrane extraction of carboxylic and hydroxycarboxylic acids by α-aminomethylphosphine oxides and other functionalized phosphoryl reagents.

The selectivity towards acetic acid found by use in the series of β-aminophosphoryl compounds, for instance, of dibutyl 2-(dioctylamino)ethylphosphonate **4**, suggests that the compounds of this type can be used for the extraction, concentrating, and separation of acidic substrates from natural and technological sources. However, it is evident that the necessary condition for the efficiency of their use is the achievement of an optimum hydrophilic—lipophilic balance by the introduction of the corresponding substituents to the potential coordination sites.

## Experimental

NMR spectra were recorded on Bruker AMX-300 and Bruker AMX-400 spectrometers in $CDCl_3$ solutions using the signal from residual protons of the deuterated solvent as an internal standard (for $^1H$ and $^{13}C$, relative to $Me_4Si$) and 85% $H_3PO_4$ as an external standard for the $^{31}P$ NMR spectra. IR spectra were obtained on a Magna-IR 750 FT-IR spectrometer (Nicolet) (resolution 2 $cm^{-1}$, number of scans 128, KBr pellets or thin layer).

Acidic dissociation constants were determined by a known procedure.[20] The apparatus and procedure for studying membrane transport were described.[4] The MFFK-4 filters (Vladipor) with the pore size 0.6 μm impregnated with solutions of carriers in phenylcyclohexane were used as impregnated membranes. The initial concentration of carboxylic acids in the donating solution and the concentration of carriers in the membrane phase were 0.1 mol $L^{-1}$. The computer processing of analytical data was performed using the VisualBasic original program developed by us at the Kazan (Volga Region) Federal University.

The synthesis method and physicochemical characteristics of *N*-octyl(dioctylmethyl)phosphine oxide (**8**) have been described earlier.[22]

**β-Aminophosphoryl compounds 1—7 (general procedure).** A stoichiometric amount of diphenylvinylphosphine oxide or diethyl or dibutyl vinylphosphonate (1 mmole for the synthesis of compounds **1**—**5** or 2 mmoles in the case of compounds **6** and **7**) was added to a solution of the corresponding amine (1 mmol) in water (2 mL) at ~20 °C. The reaction mixture was stirred for an indicate time interval at ~20 or 100 °C (see further). After the end of the reaction, the solvent was removed *in vacuo*. After lyophilic drying, compounds **1—3**, **5**, and **6** had purity >98% (NMR spectral data). In the case of compounds **4** and **7**, additional purification by column chromatography ($SiO_2$, $CHCl_3$—EtOH (100 : 3)) was carried out.

**[2-(Hexylamino)ethyl]diphenylphosphine oxide (1).** Reaction conditions: 5 h at 100 °C. The yield was 91% (after lyophilic drying), white powder, m.p. 69—71 °C. $^{31}P$ NMR ($CDCl_3$), δ: 31.35. $^1H$ NMR ($CDCl_3$), δ: 0.83 (t, 3 H, Me в $C_6H_{13}$, $^3J_{H,H}$ = = 6.5 Hz); 1.21 (br.s, 6 H, $CH_2$); 1.34—1.39 (m, 2 H, $CH_2$); 2.06 (br.s, 1 H, NH); 2.47—2.53 (m, 4 H, $PCH_2 + CH_2$); 2.91 (quintet, 2 H, $CH_2N$, $^3J_{P,H}$ = 10.8 Hz, $^3J_{H,H}$ = 7.6 Hz); 7.41—7.50, 7.65—7.73 (both m, 6 H + 4 H, Ph). $^{13}C$ NMR ($CDCl_3$), δ: 13.74 (s, Me); 22.24 (s, $CH_2$); 26.60 (s, $CH_2$); 29.53 (s, $CH_2$); 29.97 (d, $PCH_2$, $^1J_{P,C}$ = 70.8); 31.38 (s, $CH_2$); 42.56 (s, $CH_2N$); 49.39 (s, $NCH_2$ in $C_6H_{13}$); 128.37 (d, *m*-PhP, $^3J_{P,C}$ = 11.6 Hz); 130.36 (d, *o*-PhP, $^2J_{P,C}$ = 9.4 Hz); 131.47 (d, *p*-PhP, $^4J_{P,C}$ = = 2.6 Hz); 132.66 (d, *ipso*-C, $^1J_{P,C}$ = 98.9 Hz). IR (KBr), ν/$cm^{-1}$: 517, 522, 697, 719, 752, 791, 962, 1071, 1103, 1119, 1180 (P=O), 1436, 1479, 2756, 2805, 2853, 2916, 3295 (NH). Found (%): C, 72.88; H, 8.69; N, 4.17. $C_{20}H_{28}NOP$. Calculated (%): C, 72.92; H, 8.57; N, 4.25.

**Dibutyl 2-(hexylamino)ethylphosphonate (2).** Reaction conditions: 24 h at 20 °C. The yield was 95% (after lyophilic drying), yellow oil. $^{31}P$ NMR ($CDCl_3$), δ: 30.66. $^1H$ NMR ($CDCl_3$), δ: 0.84 (t, 3 H, Me in $C_6H_{13}$, $^3J_{H,H}$ = 6.7 Hz); 0.91 (t, 6 H, Me, $^3J_{H,H}$ = 7.4 Hz); 1.22—1.29 (m, 6 H, $CH_2$); 1.39 (sextet, 4 H, $C\underline{H}_2Me$ in Bu, $^3J_{H,H}$ = 7.4 Hz); 1.47 (br.t, 2 H, $NCH_2C\underline{H}_2$ in $C_6H_{13}$, $^3J_{H,H}$ = 7.0 Hz); 1.61 (quintet, 4 H, $OCH_2C\underline{H}_2$, $^3J_{H,H}$ = = 7.4 Hz); 1.98 (dt, 2 H, $PCH_2$, $^2J_{P,H}$ = 18.2 Hz, $^3J_{H,H}$ = = 7.3 Hz); 2.58 (t, 2 H, $NHCH_2$ in $C_6H_{13}$, $^3J_{H,H}$ = 7.2 Hz); 2.88 (quintet, 2 H, $CH_2N$, $^3J_{P,H}$ = 14.6 Hz, $^3J_{H,H}$ = 7.3 Hz); 3.95—3.99 (m, 4 H, $OCH_2$). IR (thin layer), ν/$cm^{-1}$: 792, 966, 1025 (P—O—C), 1068, 1246 (br, P=O), 1380, 1467, 2873, 2917, 2951, 3306 (NH), 3439. Found (%): C, 59.79; H, 11.29; P, 9.64. $C_{16}H_{36}NO_3P$. Calculated (%): C, 59.69; H, 11.44; P, 9.42.

**Dibutyl 2-(decylamino)ethylphosphonate (3).** Reaction conditions: 7 days at 20 °C. The yield was 98% (after lyophilic drying), light yellow oil. $^{31}P$ NMR ($CDCl_3$), δ: 30.60. $^1H$ NMR ($CDCl_3$), δ: 0.79 (t, 3 H, Me in $C_{10}H_{21}$, $^3J_{H,H}$ = 6.6 Hz); 0.86 (t, 6 H, Me, $^3J_{H,H}$ = 7.4 Hz); 1.18—1.20 (m, 14 H, $CH_2$); 1.31—1.39 (two overlapped m, 4 H + 2 H, $C\underline{H}_2Me$ in Bu and $NHCH_2C\underline{H}_2$ in $C_{10}H_{21}$); 1.57 (quintet, 4 H, $OCH_2C\underline{H}_2$, $^3J_{H,H}$ = = 6.8 Hz); 1.90 (dt, 2 H, $PCH_2$, $^2J_{P,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.3 Hz); 2.51 (t, 2 H, $NCH_2$ in $C_{10}H_{21}$, $^3J_{H,H}$ = 7.2 Hz); 2.81 (quintet,

2 H, $CH_2N$, $^3J_{P,H}$ = 15.0 Hz, $^3J_{H,H}$ = 7.2 Hz); 3.90—3.99 (m, 4 H, $OCH_2$). $^{13}C$ NMR ($CDCl_3$), δ: 12.08 (s, Me in Bu); 12.57 (s, Me в $C_{10}H_{21}$); 17.32 (s, $\underline{C}H_2Me$ in Bu); 21.22 (s, $\underline{C}H_2Me$ in $C_{10}H_{21}$); 24.85 (d, $PCH_2$, $^1J_{P,C}$ = 139.0 Hz); 25.93 (s, $CH_2$); 27.91 (s, $CH_2$); 28.18 (s, 2 $CH_2$); 28.20 (s, 2 $CH_2$); 28.57 (s, $CH_2$); 30.48 (s, $NHCH_2\underline{C}H_2$ in $C_{10}H_{21}$), 31.19 (d, $POCH_2\underline{C}H_2$, $^3J_{P,C}$ = 5.6 Hz); 41.95 (s, $NHCH_2$ in $C_{10}H_{21}$); 48.15 (s, $CH_2N$); 63.52 (s, $OCH_2$); 63.58 (s, $OCH_2$). IR (thin layer), ν/cm$^{-1}$: 840, 899, 979, 1025 (P—O—C), 1069, 1243 (P=O), 1379, 1466, 2854, 2926, 2957, 3305 (NH). Found (%): C, 63.55; H, 11.94; P, 7.95. $C_{20}H_{44}NO_3P$. Calculated (%): C, 63.63; H, 11.75; P, 8.20.

**Dibutyl 2-(dioctylamino)ethylphosphonate (4).** Reaction conditions: 18 h at 100 °C. The yield was 81% (after column chromatography), light yellow oil. $^{31}P$ NMR ($CDCl_3$), δ: 31.35. $^1H$ NMR ($CDCl_3$), δ: 0.85 (t, 6 H, Me in $C_6H_{13}$, $^3J_{H,H}$ = 6.9 Hz); 0.91 (t, 6 H, Me, $^3J_{H,H}$ = 7.5 Hz); 1.24 (br.s, 20 H, $CH_2$); 1.35—1.42 (two overlapped m, 4 H + 4 H, $C\underline{H}_2Me$ in Bu and $NCH_2C\underline{H}_2$ in $C_8H_{17}$); 1.62 (quintet, 4 H, $OCH_2C\underline{H}_2$, $^3J_{H,H}$ = 6.7 Hz); 1.87 (dt, 2 H, $PCH_2$, $^2J_{P,H}$ = 19.1 Hz, $^3J_{H,H}$ = 8.0 Hz); 2.35 (t, 4 H, $NCH_2$ in $C_8H_{17}$, $^3J_{H,H}$ = 7.5 Hz); 2.73—2.79 (m, 2 H, $CH_2N$); 3.95—4.04 (m, 4 H, $OCH_2$). $^{13}C$ NMR ($CDCl_3$), δ: 13.27 (s, Me in Bu); 13.75 (s, Me in $C_8H_{17}$); 18.40 (s, $\underline{C}H_2Me$ in Bu); 21.86 (d, $PCH_2$, $^1J_{P,C}$ = 136.9 Hz); 22.33 (s, $\underline{C}H_2Me$ in $C_8H_{17}$); 26.61 (s, $CH_2$); 27.18 (s, $CH_2$); 28.97 (s, $CH_2$); 29.21 (s, $CH_2$); 31.52 (s, $CH_2$); 32.25 (d, $POCH_2\underline{C}H_2$, $^3J_{P,C}$ = 6.2 Hz); 46.22 (s, $CH_2N$); 53.05 (s, $NCH_2$ in $C_8H_{17}$); 64.92 (s, $OCH_2$); 64.98 (s, $OCH_2$). IR (thin layer), ν/cm$^{-1}$: 805, 852, 900, 965, 1024 (P—O—C), 1065, 1119, 1242 (ш, P=O), 1308, 1380, 1438, 1466, 2864, 2925, 2957. Found (%): C, 67.84; H, 12.27; P, 6.55. $C_{26}H_{56}NO_3P$. Calculated (%): C, 67.64; H, 12.23; P, 6.71.

**[2-(Dioctylamino)ethyl]diphenylphosphine oxide (5).** Reaction conditions: 18 h at 100 °C. The yield was 90% (after lyophilic drying), viscous light yellow oil. $^{31}P$ NMR ($CDCl_3$), δ: 31.57. $^1H$ NMR ($CDCl_3$), δ: 0.84 (t, 6 H, Me, $^3J_{H,H}$ = 6.8 Hz); 1.20 (br.s, 16 H, $CH_2$); 1.21—1.31 (m, 8 H, $CH_2$); 2.32 (t, 4 H, $NCH_2$ in $C_8H_{17}$, $^3J_{H,H}$ = 7.0 Hz); 2.36—2.43 (m, 2 H, $PCH_2$); 2.77—2.81 (m, 2 H, $CH_2N$); 7.43—7.44, 7.69—7.74 (both m, 6 H + 4 H, Ph). $^{13}C$ NMR ($CDCl_3$), δ: 13.44 (s, Me); 21.96 (s, $CH_2$); 25.89 (d, $PCH_2$, $^1J_{P,C}$ = 69.3 Hz); 26.41 (s, $CH_2$); 26.71 (c, $CH_2$); 28.60 (c, $CH_2$); 28.83 (s, $CH_2$); 31.16 (s, $CH_2$); 45.24 (s, $CH_2N$); 52.84 (s, $NCH_2$ in $C_8H_{17}$); 127.91 (d, *m*-PhP, $^3J_{P,C}$ = 11.8 Hz); 129.97 (d, *o*-PhP, $^2J_{P,C}$ = 9.5 Hz); 130.96 (d, *p*-PhP, $^4J_{P,C}$ = 2.2 Hz); 132.53 (d, *ipso*-C, $^1J_{P,C}$ = 98.5 Hz). IR (thin layer), ν/cm$^{-1}$: 515, 545, 697, 718, 736, 1120, 1184 (sh, P=O), 1438, 1467, 2807, 2854, 2925, 3056, 3422 (ш, $H_2O$). Found (%): C, 75.01; H, 10.33; N, 2.94. $C_{30}H_{48}NOP \cdot 0.5H_2O$. Calculated (%): C, 75.27; H, 10.32; N, 2.93.

***N,N*-Di[2-(dibutoxyphosphoryl)ethyl]hexylamine (6).** Reaction conditions: 40 h at 100 °C. The yield was 90% (after lyophilic drying), light yellow oil. $^{31}P$ NMR ($CDCl_3$), δ: 30.77. $^1H$ NMR ($CDCl_3$), δ: 0.91 (t, 3 H, Me in $C_6H_{13}$, $^3J_{H,H}$ = 6.9 Hz); 0.97 (t, 12 H, Me, $^3J_{H,H}$ = 7.1 Hz); 1.29 (br.s, 6 H, $CH_2$); 1.37—1.49 (m, 8 H + 2 H, $C\underline{H}_2Me$ in Bu and $NCH_2C\underline{H}_2$ in $C_6H_{13}$); 1.62—1.72 (two overlapped m, 8 H, $OCH_2C\underline{H}_2$, $^3J_{H,H}$ = 6.8 Hz); 1.86—1.98 (m, 4 H, $PCH_2$); 2.41 (t, 2 H, $NCH_2$ in $C_6H_{13}$, $^3J_{H,H}$ = 7.3 Hz); 2.75—2.82 (m, 4 H, $CH_2N$); 3.99—4.09 (m, 8 H, $OCH_2$). $^{13}C$ NMR ($CDCl_3$), δ: 13.13 (s, Me in Bu); 13.57 (s, Me in $C_6H_{13}$); 18.34 (s, $\underline{C}H_2Me$ in Bu); 22.17 (s, $\underline{C}H_2Me$ in $C_6H_{13}$); 22.59 (d, $PCH_2$, $^1J_{P,C}$ = 137.7 Hz); 26.61 (s, $CH_2$); 26.69 (s, $CH_2$); 31.32 (s, $CH_2$); 32.17 (d, $POCH_2\underline{C}H_2$, $^3J_{P,C}$ = 6.1 Hz); 45.94 (s, $CH_2N$); 52.47 (s, $NCH_2$ in $C_6H_{13}$); 64.66 (s, $OCH_2$); 64.73 (s, $OCH_2$). IR (thin layer), ν/cm$^{-1}$: 979, 1024 (P—O—C), 1067, 1238 (br, P=O), 1381, 1466, 2874, 2933, 2959, 3459 (br, $H_2O$). Found (%): C, 57.60; H, 10.60; P, 11.21. $C_{26}H_{57}NO_6P_2$. Calculated (%): C, 57.65; H, 10.61; P, 11.44.

***N,N*-Di[2-(diethoxyphosphoryl)ethyl]hexylamine (7).** Reaction conditions: 4 h at 100 °C. The yield was 75% (after column chromatography), light yellow oil. $^{31}P$ NMR ($CDCl_3$), δ: 30.70. $^1H$ NMR, δ: 0.84 (t, 3 H, Me in $C_6H_{13}$, $^3J_{H,H}$ = 7.0 Hz); 1.22—1.24 (m, 6 H, $CH_2$); 1.28 (t, 12 H, Me, $^3J_{H,H}$ = 7.1 Hz); 1.35—1.38 (m, 2 H, $CH_2$); 1.85 (dt, 4 H, $PCH_2$, $^2J_{P,H}$ = 19.1 Hz, $^3J_{H,H}$ = 7.8 Hz); 2.34 (t, 2 H, $NCH_2$ in $C_6H_{13}$, $^3J_{H,H}$ = 7.0 Hz); 2.72 (quintet, 4 H, $CH_2N$, $^3J_{H,H}$ = 7.8 Hz); 4.00—4.09 (m, 8 H, $OCH_2$). IR (thin layer), ν/cm$^{-1}$: 789, 937, 960, 1032 (P—O—C), 1057, 1248 (br, P=O), 1392, 1467, 2872, 2932, 2965, 2980. Found (%): C, 48.35; H, 9.50; P, 13.50. $C_{16}H_{37}NO_6P_2 \cdot 0.2CHCl_3$. Calculated (%): C, 48.22; H, 9.16; P, 13.66.

**Dibutyl *N,N*-dioctylaminomethylphosphonate (9)** was synthesized by the Kabachnik—Fields reaction between dibutyl phosphite, dioctylamine, and formaldehyde according to the general procedure.[22] B.p. 175—176 °C/42 Pa, $n_D^{20}$ 1.4520. $^{31}P$ NMR ($CDCl_3$), δ: 25.5. $^1H$ NMR, (δ: 0.96 (t, 6 H, Me, $^3J_{H,H}$ = 7.35 Hz); 1.22—1.74 (m, 12 H + 8 H, $CH_2$); 2.55—2.64 (t, 4 H, $NCH_2$); 2.90 (d, $PCH_2$, $^2J_{P,H}$ = 10.26 Hz); 4.04—4.14 (dq, 4 H, $OCH_2$). IR (thin layer), ν/cm$^{-1}$: 1024 (P=O).

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