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Addition of Secondary Amines to Alkynephosphonates

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Abstract — Addition of secondary amines to diethyl alkynephosphonates, catalyzed by Cu(I) salts, proceeds regio- and stereospecifically and yields diethyl (*E*)-2-diethylaminooalkenephosphonates. The *E* configuration was established by analysis of the vicinal coupling constants between the phosphorus and carbon nuclei in the ^{13}C NMR spectra of the reaction products and model compounds: $^{3}J_{PC}$ is 6–10 Hz at the *cis* arrangement of the coupled nuclei and 16 Hz or higher at the *trans* arrangement. In all the diethyl diethylaminoalkenephosphonates obtained, $^{3}J_{PC}$ is about 5 Hz, suggesting *cis* addition.

2-Dialkylaminoalkenephosphonates are interesting as precursors of difficultly available Horner–Emmons reagents, β-keto and β-aldo phosphonates [1–3], as intermediates in the synthesis of various acyclic [4–7] and heterocyclic compounds [8–14], and as model compounds in studies of certain biochemical processes [15].

Methods for preparing 2-dialkylaminoalkenephosphonates were considered in detail in [16], where a general method was proposed for the synthesis of 2-dialkylaminoalkenephosphonates by the Arbuzov reaction catalyzed with Ni(II) salts. We suggest an alternative convenient route to β-enamino phosphonates: addition of amines across alkynephosphonate triple bond. This route was studied earlier with a few examples only.

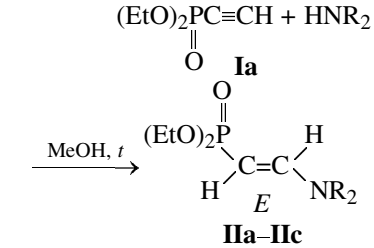
For example, as far back as 1963, diethyl (*E*)-2-diethylaminoethenephosphonate was prepared in a high yield from a mixture of ethynephosphonate and diethylamine; the reaction was accompanied by self-heating [17]. More recently, it was noted that the reactions of ethynephosphonate with secondary amines yield mixtures of (*E*)- and (*Z*)-β-enamino phosphonates [18]. Propynephosphonate adds secondary amines to form a mixture of 2-dialkylaminopropenephosphonate and 2,2-bis(dialkylamino)propanephosphonate in poor yield (10–15%) [19].

2-Alkylaminoalkenephosphonates were prepared in [17] by addition of primary amines to alkynephosphonates, but they were not isolated pure and were used in the synthesis of ketimines and aldimines, and then of unsaturated aldehydes and ketones. β-Enamino phosphonates were subsequently isolated, and their ^{1}H NMR study showed that addition of primary amines to alkynephosphonates gives a mixture of geometric isomers, while addition of a secondary amine, diethylamine, to alkynephosphonate yields a single stereochemical form, *E* isomer [20].

Addition of primary and secondary amines to ethynyldiphenylphosphine oxide, catalyzed by butyllithium and yielding the corresponding (*E*)-2-aminovinyldiphenylphosphine oxides, was studied in most detail [21]. Noncatalyzed addition of primary amines to alkynyldiphenylphosphine oxides yields a mixture of the corresponding (*E*)- and (*Z*)-aminovinylphosphine oxides [22].

We found that the reaction of secondary amines with diethyl alkynephosphonates is noticeably accelerated in the presense of catalytic amounts of Cu(I) salts. Successful use of CuCl as a catalyst was noted for addition of primary and secondary amines to nitriles; the reaction proceeded with a high yield (80–100%) [23].

In this work, we studied addition of secondary amines to diethyl alkynephosphonates in the presence of catalytic amounts of Cu(I)Cl. With diethyl ethynephosphonate as example, we found that addition of secondary amines both in the presence and in the absence of copper(I) salts proceeds as *cis* addition and yields exclusively the *E* isomer of the corresponding diethyl 2-dialkylaminoethenephosphonate.



IIa–IIc

NR_2 = NEt_2, $N(CH_2)_5$, $N[(CH_2)_2]_2O$.

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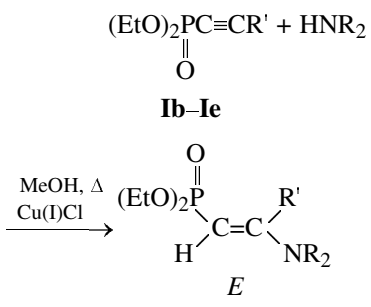
Table 1. Conditions of synthesis, yields, and constants of diethyl (*E*)-2-(dialkylamino)alkenephosphonates **IIa**–**IIm**

Comp no.	R'	Method			Time, h	Yield, %[a]	bp, °C (*P*, mm)
		NR_2	method	solvent, catalyst			
IIa	H	$N(C_2H_5)_2$	*a*	EtOH	0.5	42	109 (0.1)
IIb	H	$N(CH_2)_5$	*b*	MeOH	12	36	112 (0.1)
IIc	H	$N[(CH_2)_2]_2O$	*b*	MeOH	18	80	163 (0.5)
IId	CH_3	$N(CH_3)_2$	*b*	MeOH, Cu(I)Cl	18	72	121 (0.4)
IIe	CH_3	$N(C_2H_5)_2$	*a*	EtOH, Cu(I)Cl	2.5	38	126 (0.1)
IIf	CH_3	$N(CH_2)_5$	*b*	MeOH, Cu(I)Cl	22	41	170 (0.5)
IIg	CH_3	$N[(CH_2)_2]_2O$	*b*	MeOH, Cu(I)Cl	26	45	180 (0.5)
IIh	C_2H_5	$N(C_2H_5)_2$	*a*	Et_2O, Cu(I)Cl	9.3	36	130 (0.1)
IIi	C_2H_5	$N(CH_2)_5$	*b*	MeOH, Cu(I)Cl	26.5	35	156 (0.2)
IIj	C_6H_5	$N(CH_3)_2$	*b*	MeOH, Cu(I)Cl	30	64	155 (0.4)
IIk	C_6H_5	$N(C_2H_5)_2$	*a*	EtOH, Cu(I)Cl	3.5	41	156 (0.1)
III	C_6H_5	$N(CH_2)_5$	*b*	MeOH, Cu(I)Cl	50	40	160 (0.1)
IIm	C_6H_5	$N[(CH_2)_2]_2O$	*b*	MeOH, Cu(I)Cl	57	38	165 (0.1)

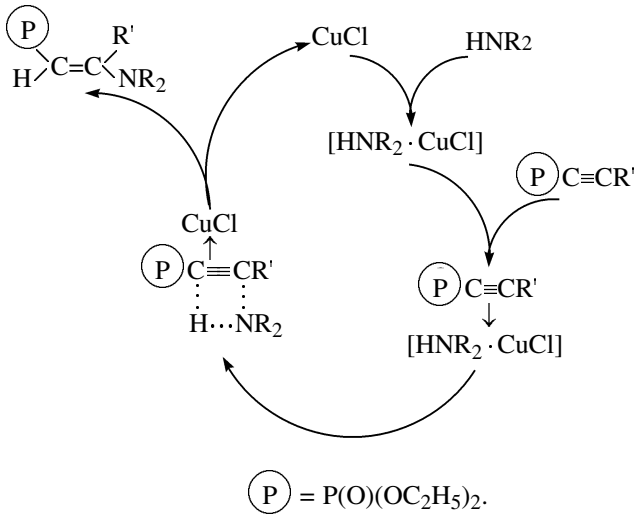
[a] According to the ^1H NMR spectrum, the products are formed in quantitative yield, but the yields of the isolated products are considerably lower because of partial saponification and thermolysis during high-temperature distillation.

Secondary amines do not react with substituted diethyl ethynephosphonates in the absence of Cu(I)Cl at a noticeable rate even on heating in ampule to 120°C. At a higher temperature (~150°C), the alkynephosphonates polymerize. Addition of catalytic amounts of copper(I) salts allows the addition under mild conditions, and the reaction proceeds regio- and stereospecifically with formation of the corresponding diethyl (*E*)-diethylaminooalkenephosphonates (Table 1).



R' = Me, Et, Ph, *t*-Bu; NR_2 = NMe_2, NEt_2, $N(CH_2)_5$, $N[(CH_2)_2]_2O$.

Presumably, in the first step the amine coordinates with Cu(I)Cl, which is manifested as strong coloration of the reaction solution. Then copper in the amine complex coordinates with the π electrons of the alkynephosphonate triple bond [24], which promotes *cis* addition of the amine and leads to formation of the corresponding diethyl (*E*)-diethylaminoalkenephosphonate and release of Cu(I)Cl (see scheme).



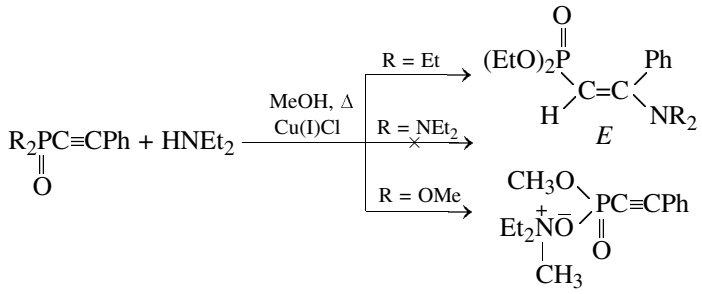
In nonpolar solvents such as carbon tetrachloride and benzene, no reaction occurred; in polar chloroform and isobutyl alcohol, the reaction was slow. According to the ^1H NMR data obtained using ^1H–$\{^{31}P\}$ NMDR technique, the reaction in chloroform gives traces of the addition products. In diethyl ether, methanol, and ethanol, these reactions proceed with quantitative yield. The similar effect of solvents was noted in the study of amine addition to alkynediphenylphosphine oxides [22] and nitriles [23] in polar media.

As the compounds formed are hygroscopic, it is necessary to use anhydrous solvents; from the viewpoint of ensuring anhydrous conditions, the best choice is reaction in absolute methanol in sealed ampules.

Attempts to perform the reaction without a solvent with excess amine resulted in extensive tarring and various transformations of both the addition products and starting material: cleavage of the P–C bond in the β-enamino phosphonate formed, partial replacement of ethoxy group by diethylamino group, and other processes.

The reactivity of alkynephosphonates depends regularly on the electronic and steric effects of substituent at the triple bond. Replacement of Me by Ph and Et decelerates the addition, and with R' = *t*-Bu the reaction does not occur at all.

The type of substituent at the phosphorus atom also affects the course of this reaction. For example, substitution of alkyl or amide groups for the ester group decelerates the reaction considerably. Diethyl(2-phenylethynyl)phosphine oxide reacts slowly with formation of diethyl(2-diethylamino-2-phenylethenyl)phosphine oxide, and the reaction of phenylethynephosphonic bis(diethylamide) yields no addition compound. In the case of dimethyl alkynephosphonate, an ammonium salt is formed, and further addition of the amine does not occur.



The structure of the obtained diethyl diethylaminoalkenephosphonates **IIa**–**IIm** was confirmed unambiguously by their ^{1}H, ^{13}C, ^{31}P NMR and IR spectra. The IR spectra contain absorption bands at ~1560 (C=C) and ~1215 cm^{-1} (P=O). The ^{31}P resonance (δ_P ~23-29 ppm) occurs in the range characteristic of four-coordinate phosphorus atom. The ^{1}H NMR spectra of enamines **IIa**–**IIm** show proton signals of CH groups in the region of ~4 ppm ($^2J_{HP}$ 9–12 Hz) (Table 2), but not 5–7 ppm [25], confirming attack of the amino group at the carbon atom remote from phosphorus. The ^{13}C NMR spectra of diethyl diethylaminoalkenephosphonates **IIa**–**IIm** are characterized by a significant difference between the chemical shifts of the C^1 (71–84 ppm) and C^2 (152–166 ppm) atoms (Table 3), which is due to high polarization of the double bond in these compounds. Thus, our results show that the reaction is regioselective, yielding exclusively 2-amino derivatives.

Determination of the geometric configuration of diethyl diethylaminooalkenephosphonates **IIa**–**IIm** involved certain problems. For recently prepared diethyl (2-piperidino-2-phenylethene)phosphonate, the geometry was not determined exactly [16]. To elucidate the structure of β-enamino phosphonates **IIa**–**IIm**, we used the well-known dependence of the vicinal coupling constant ^3J on the geometric configuration of the compound: in alkene derivatives, this constant is commonly larger for the *trans* (compared to *cis*) arrangement of the nuclei. This trend, known for H–H [26] and H–P [25] coupling, was used, in particular, in our previous studies. However, the steric dependence of $^3J_{PC}$, which might be used in this work, was not studied previously in detail, and data are available for a few examples only. Therefore, we synthesized a series of model compounds with known geometry and measured their ^{13}C NMR spectra (Table 4).

Analysis of the vicinal constants $^3J_{PC}$ of model compounds showed that, at *trans* configuration, these constants range from 16 to 24 Hz, and at *cis* configuration, from 6 to 10 Hz (Table 4). Thus, the vicinal $^3J_{PC}$ constant is stereospecific, and the values for the two isomers do not overlap. This allows determination of the geometry at the double bind even when only one isomer is taken for the study.

The ^{13}C NMR spectra of diethyl diethylaminoalkenephosphonates **IId**–**IIi** show doublets in the region of ~17.0–23.5 ppm of the CH_3 and CH_2 carbon atoms, with $^3J_{PC}$ ~3–5 Hz. In the spectra of **IIj**–**IIm**,

Table 2. IR, ^{1}H NMR, and ^{31}P NMR data for diethyl (*E*)-2-(dialkylamino)alkenephosphonates (*E*)-$(C_2H_5O)_2$·P(O)CH_A=C$(NR_2)H_B$ (**IIa**–**IIc**) and (*E*)-$(C_2H_5O)_2$P(O)·CH_A=C(NR_2)R' (**IIa**–**IIm**)

Comp. no.	IR spectrum, ν(C=C), cm^{-1}	^{1}H NMR spectrum, δ(H_A), ppm ($^2J_{HP}$, $^3J_{HH}$, Hz)/ δ(H_B), ppm ($^3J_{HP}$, Hz)	^{31}P NMR spectrum, δ_P, ppm
IIa	1593	3.6 (11.5, 14.5)/6.8 (16.0)	29.2
IIb	1596	4.1 (6.0, 14.8)/6.9 (15.3)	29.5
IIc	1600	4.2 (12.0, 14.5)/6.9 (14.8)	27.6
IId	1554	3.6 (9.4)	27.2
IIe	1558	3.5 (9.8)	27.5
IIf	1560	3.9 (9.8)	27.9
IIg	1560	3.8 (9.0)	26.0
IIh	1546	3.5 (9.8)	27.2
IIi	1629	3.9 (10.3)	27.3
IIj	1534	4.1 (9.8)	24.1
IIk	1533	3.9 (10.3)	24.1
IIl	1540	4.4 (9.8)	24.6
IIm	1540	4.4 (9.2)	23.1

Table 3. ^{13}C NMR data (δ_C, ppm; *J*, Hz) for diethyl (*E*)-2-(dialkylamino)alkenephosphonates (*E*)-$(C_2H_5O)_2$P(O)·CH=C(NR_2)R' (**IIa**–**IIm**)[a]

Comp. no.	δ_1	δ_2	δ_3	$^1J_{PC}$	$^2J_{PC}$	$^3J_{PC}$
IIa	71.5	152.1	–	208.0	20.8	–1
IIb	72.4	153.5	–	209.2	20.1	–1
IIc	75.5	153.6	–	201.3	19.3	–1
IId	73.8	160.8	17.4	215.6	20.2	4.21
IIe	73.0	158.8	17.2	217.3	21.0	5.01
IIf	76.0	160.1	17.4	212.7	19.3	3.61
IIg	79.2	160.6	17.0	212.9	19.2	2.81
IIh	72.5	164.4	22.3	217.3	21.6	5.11
IIi	75.6	166.0	23.5	215.7	21.7	5.21
IIj	78.5	163.6	135.7	215.6	18.0	7.51
IIk	76.6	161.2	135.2	217.8	17.1	5.61
IIl	81.2	164.1	136.5	214.4	17.4	4.11
IIm	83.9	163.8	135.2	212.6	16.3	4.1

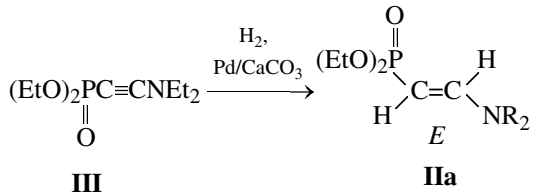
[a] The following numbering of carbon atoms was used: $(C_2H_5O)_2P(O)C^1H=C^2(X)(R')^3$; in the case of R' = Ph, by the C^3 atom is meant the *ipso* carbon atom of the aromatic ring.

the *ipso* carbon atoms of aromatic ring resonate at 135.2–136.5 ppm, $^3J_{PC}$ 4–7.5 Hz (Table 3). That is, the vicinal coupling constant is small and hence the β-enamino phosphonates obtained can be unambiguously identified as the products of *cis* addition, i.e., as *E* isomers of the corresponding diethyl diethylaminoalkenephosphonates.

The geometry of diethyl 2-dialkylaminopropenephosphonates can also be determined from the allyl coupling constant $^4J_{HP}$. In diethyl 2-dialkylaminopropenephosphonates **IId**–**IIg**, $^4J_{HP}$ is ~1.5 Hz, which is typical of cisoid arrangement; the transoid constant commonly ranges from 0 to 0.5 Hz [25]. The *E* configuration of diethyl 2-dialkylaminoethenephosphonates **IIa**–**IIc** was established from $^3J_{HH}$ and $^3J_{HP}$, which were ~14.5 and 15–16 Hz, respectively (cf. $^3J_{HH}^{cis}$ 10–12, $^3J_{HH}^{trans}$ ~14–17; $^3J_{HP}^{cis}$ ~15–17, $^3J_{HP}^{trans}$ ~45–60 Hz [13, 25]).

The structures of **IIe** and **IIh** were confirmed by a ^{1}H NMR study using lanthanide shift reagents. We used europium tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate) Eu(fod)$_3$. The lanthanide coordinates at the phosphoryl oxygen atom and induces various shifts of the proton signals depending on the location of the group relative to the phosphoryl fragment. Comparison of the ^{1}H NMR data for diethyl 2-diethylaminoprop-1-enephosphonate and diethyl diethylaminobut-1-enephosphonate, obtained in the presence and in the absence of the lanthanide shift reagent, shows that the lanthanide shift of the proton signals of the CH_2 and CH_3 groups is considerably larger than that of the signal of CH_2 protons in the amino group. Hence, the amino group is more distant from the phosphoryl group than the ethyl and methyl groups and therefore is less affected by the lanthanide. This confirms the *E* configuration of the phosphonates under consideration.

For comparison of the spectroscopic data, we attempted to prepare authentic diethyl (*Z*)-2-diethylaminoethenephosphonate by hydrogenation of the corresponding ynamino phosphonate on Pd/$CaCO_3$. Similarly to the hydrogenation of other acetylenic phosphonates [28], we expected formation of diethyl (*Z*)-2-diethylaminoethenephosphonate. However, all the experiments resulted in formation of the same diethyl (*E*)-2-diethylaminoethenephosphonate with the spectral characteristics coinciding with those of the addition compound obtained from diethyl ethynephosphonate and diethylamine.



III **IIa**

Table 4. ^{13}C NMR data (δ_C, ppm; J, Hz) for model and known compounds $(C_2H_5O)_2P(O)CH=C(X)R'$ [a]

No.	R'	X	Isomer	δ_1	δ_2	δ_3	$^1J_{PC}$	$^2J_{PC}$	$^3J_{PC}$
1	Me	H	*Z*	116.8	148.6	15.6	188.7	5.0	10.4
2	Ph	H	*Z*	115.5	147.3	134.3	184.2	5.9	7.0
3	*t*-Bu	H	*Z*	113.3	161.2	33.3	186.2	4.7	6.3
4	Ph	NHCONHPh	*E*	90.0	152.7	136.5	205.0	–	6.1 [4]
5	Ph	$NHCONHC_3H_7$	*E*	89.6	155.5	137.0	205.5	–	6.1 [4]
6	Ph	$NHCONHPhOCH_3$	*E*	89.8	155.2	136.6	204.0	–	6.0 [4]
7	Me	NHBu-*t*	*E*	74.5	156.5	21.3	213.8	–	5.2 [14]
8	Me	$NHCH_2CH=CH_2$	*E*	70.3	159.4	18.1	213.1	–	4.2 [14]
9	Me	$NHCH(Ph)CH_3$	*E*	72.5	157.4	18.4	213.9	–	4.8 [14]
10[b]	Me	NHBu-*t*	*E*	80.6	156.8	22.4	128.0	–	7.0 [14]
11[b]	Me	$NHCH_2Ph$	*E*	79.0	159.2	19.3	129.0	–	5.5 [14]
12[b]	Me	H	*Z*	122.1	149.3	16.8	101.0	0.0	7.3 [27]
13[b]	Ph	H	*Z*	121.6	149.8	134.6	98.2	<2	6.9 [27]
14	Me	Me	–	111.7	158.4	20.2	189.5	10.7	6.5
							27.3		24.2
15	Me	H	*E*	116.3	148.9	19.4	188.6	5.0	23.8
16[c]	Me	Cl	*Z*	122.3	154.8	29.9	175.3	6.0	19.3
17	Ph	H	*E*	113.5	147.7	134.5	191.6	6.7	23.7
18	Ph	Cl	*Z*	112.7	149.6	136.6	199.1	3.2	16.4
19	*t*-Bu	H	*E*	111.0	161.9	33.7	188.0	3.5	20.1
20	*t*-Bu	Cl	*Z*	111.5	163.2	40.7	196.9	2.5	12.5
21[c]	*t*-Bu	Cl	*Z*	119.4	167.4	41.3	160.5	7.5	14.9
22	Ph	NHCONHPh	*Z*	92.2	151.7	137.9	184.3	–	19.1 [4]
23	Ph	$NHCONHC_3H_7$	*Z*	91.0	153.9	138.0	183.8	–	18.6 [4]
24[b]	Me	NHBu-*t*	*Z*	74.9	162.8	23.3	116.0	–	15.1 [14]
25[b]	Me	$NHCH_2Ph$	*Z*	75.7	162.5	20.4	115.1	–	15.1 [14]
26	Me	NHBu-*t*	*Z*	72.5	163.7	22.9	191.0	–	21.1 [14]
27	Me	$NHCH_2CH=CH_2$	*Z*	70.1	162.9	20.4	198.7	–	21.0 [14]
29[b]	Me	H	*E*	123.7	147.6	19.9	102.8	1.9	18.3 [27]
30[b]	Ph	H	*E*	119.1	147.3	134.8	103.7	3.7	18.4 [27]
31	Ph	NHPh	*Z*	84.2	–	137.1	187.3	–	19.6 [13]
32	Ph	NHPhCl-4	*Z*	84.6	–	136.6	187.7	–	19.7 [13]
33	Ph	$NHPhCF_3$-3	*Z*	84.2	–	136.3	186.3	–	19.1 [13]

[a] The following numbering of carbon atoms was used: $(C_2H_5O)_2P(O)C^1=C^2X(R')^3$; in the case of R' = Ph, by the C^3 atom is meant the *ipso* carbon atom of the aromatic ring. [b] Acid chlorides. [c] Diphenylphosphine oxide derivatives.

To confirm additionally the structure of the addition compounds obtained, we synthesized diethyl 2-diethylaminoprop-1-enphosphonate by reaction of diethyl allenephosphonate with diethylamine in carbon tetrachloride. The spectral characteristics of the compound obtained coincided with those of **IIe**.

The synthesized β-enamino phosphonates **IIa**–**IIm** are yellow oily liquids stable in a dry atmosphere.

We also found that diethyl diethylaminooalkenephosphonates can be prepared from the corresponding diethyl 2-chloroalkenephosphonates with formation of the same diethyl (*E*)-diethylaminooalkenephosphonates, but in a lower yield.

$$\underset{\textbf{IV}}{(EtO)_2P(O)CH=CClR'} + 2Et_2NH \longrightarrow \underset{\textbf{Ib, Id}}{[(EtO)_2P(O)C\equiv CR']}$$

$$(E)\text{-}(EtO)_2P(O)CH=C(NEt_2)R' + [EtNH_3]^+Cl^-,$$
$$\textbf{IId, IIk}$$

R' = Me, Ph.

The ^1H NMR spectra of the reaction mixtures, taken using the ^1H–{^{31}P} NMDR technique, contain the signals characteristic of the corresponding diethyl alkynephosphonates. This fact suggests that the first step of this reaction is HCl elimination with formation of the corresponding acetylenic compound **Ib** or **Id**, which in the second step adds amine. This reaction

also gives diethyl (*E*)-diethylaminooalkenephosphonates. This method is an alternative route to diethyl diethylaminooalkenephosphonates.

Diethyl diethylaminooalkenephosphonates **IId**–**IIm** can be hydrolyzed with formation of the corresponding β-keto phosphonates, which are interesting as Horner–Emmons reagents [1–3], as synthetic intermediates [29–31], and as the effective metal extractants [32].

$$\underset{\textbf{IId–IIm}}{(EtO)_2P(O)CH{=}C(NR_2)R'} + H_2O \rightarrow \underset{\textbf{Va–Vc}}{(EtO)_2P(O)CH_2C(O)R'},$$

R' = Me, Et, Ph; NR_2 = NMe_2, NEt_2, $N(CH_2)_5$, $N[(CH_2)_2]_2O$.

Hydrolysis of diethyl 2-dialkylaminoethenephosphonates yields phosphonamides, which may be interesting for pharmacology [33, 34], as intermediates in the synthesis of α,β-unsaturated amides [35], and as extractants for transplutonium and rare-earth elements [36, 37]. It is known that several diethoxyphosphorylacetamides exhibit strong physiological activity and have properties of strong system acaricides [38].

$$\underset{\textbf{IIa–IIc}}{(EtO)_2P(O)CH{=}C(NR_2)H} + H_2O \longrightarrow \underset{\textbf{VIa–VIc}}{(EtO)_2P(O)CH_2C(O)NR_2},$$

NR_2 = NEt_2, $N(CH_2)_5$, $N[(CH_2)_2]_2O$.

The structure of β-keto phosphonates and phosphonamides was confirmed by the set the ^1H, ^{13}C, ^{31}P NMR and IR data and by comparison of their characteristics with published data [39–41].

Thus, we suggested a general and convenient procedure for preparing various diethyl (*E*)-diethylaminooalkenephosphonates by addition of secondary amines to diethyl alkynephosphonates in the presence of catalytic amounts of Cu(I)Cl. New β-enamino phosphonates **IIb**, **IIc**, and **IIf**–**IIm** were prepared. Addition of secondary amines to diethyl alkynephosphonates is shown to proceed regio- and stereoselectively with exclusive formation of diethyl (*E*)-2-dialkylaminoalkenephosphonates. The vicinal constant $^3J_{PC}$ is stereospecific and can be used to determine the geometry of 2-aminoalkenephosphonates. Alternatively, diethyl diethylaminoalkenephosphonates can be prepared by reactions of secondary amines with 2-chloroalkenephosphonates; preparative hydrolysis of diethyl diethylaminoalkenephosphonates can be used as route to difficultly accessible keto phosphonates and phosphonamides, which are interesting as the Horner–Emmons reagents.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 instrument in a thin layer on KBr. The ^1H NMR spectrum recorded using ^1H–{^{31}P} NMDR technique was taken on a Tesla BS-497 instrument (100 MHz), with HMDS as internal reference. The ^1H, ^{31}P, and ^{13}C NMR spectra were taken on a Bruker AC-200 instrument (internal reference $CDCl_3$, external reference 85% H_3PO_4, solvent $CDCl_3$). The mass spectra were taken on a Hewlett–Packard-5890II instrument.

In the experiments we used absolute solvents. Other chemicals were distilled when necessary. All the reactions were performed in an argon flow.

The starting alkynephosphonates were prepared by procedures described in [17, 42–44]. The physicochemical constants of **Ia**–**Ie** agreed with published data [45–48].

Diethyl (*E*)-diethylaminoalkenephosphonates IIa–IIm. *a*. A solution of 0.01 mol of appropriate alkynephosphonate and 0.011 mol of secondary amine in 10 ml of appropriate solvent, and, in some experiments, 0.05 g of Cu(I)Cl were placed in a flask equipped with a reflux condenser; the mixture was refluxed for several hours under argon (Table 1). The reaction progress was monitored by ^1H NMR spectroscopy; the reaction was stopped after complete consumption of the starting alkynephosphonate. Then the catalyst was filtered off, the solvent was distilled off, and the residue was distilled in a vacuum (0.1–0.5 mm).

b. 0.01 mol of appropriate alkynephosphonate, 0.011 mol of secondary amine, and, when necessary, 0.05 g of Cu(I)Cl in 2 ml of absolute methanol were heated for several hours in an ampule at 100–110°C (Table 1). The solvent was distilled off, and the residue was fractionated in a vacuum (0.1–0.5 mm).

Diethyl (*E*)-2-(diethylamino)ethenephosphonate IIa: bp 109°C (0.1 mm), n_D^{20} 1.5703. IR spectrum (KBr), ν, cm^{-1}: 2970, 1593 (C=C), 1246 (P=O), 1020. ^1H NMR spectrum, δ, ppm (CCl_4): 1.18 t (6H, CH_3), 1.26 t (6H, CH_3), 3.11 q (4H, CH_2N), 3.62 d.d (1H, CH, $^3J_{HH}$ 14.5, $^2J_{HP}$ 11.5 Hz), 3.8 q (4H, CH_2O), 6.79 d.d (1H, CH, $^3J_{HH}$ 14.5, $^3J_{HP}$ 16.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.36 (CH_3), 15.82 (CH_3), 39.97 (CH_2N), 60.23 (CH_2O), 71.7 d (CH, $^1J_{PC}$ 212.18 Hz), 152.09 d (=C– $^2J_{PC}$ 17.56 Hz). ^{31}P NMR spectrum, δ_P, ppm: 29.14.

Diethyl (*E*)-2-piperidinoethenephosphonate

IIb: bp 112°C (0.1 mm). ^{1}H NMR spectrum, δ, ppm: 1.28 t (6H, CH_3), 1.54 m (6H, CH_2 piperidine), 3.11 t (4H, CH_2N), 3.97 q (4H, CH_2O), 4.14 d.d (1H, CH, $^3J_{HH}$ 14.5, $^2J_{HP}$ 6 Hz), 6.93 d.d (1H, CH, $^3J_{HH}$ 14.5, $^3J_{HP}$ 15.25 Hz). ^{13}C NMR spectrum, δ_C, ppm: 15.92 (CH_3), 23.83 (*p*-CH_2, piperidine), 24.27 (*m*-CH_2, piperidine), 48.75 (CH_2N), 60.33 (CH_2O), 72.44 d (CH, $^1J_{PC}$ 209.2 Hz), 153.44 d (=C–N, $^2J_{PC}$ 20.1 Hz). ^{31}P NMR spectrum, δ_P, ppm: 29.45.

Diethyl (*E*)-2-morpholinoethenephosphonate IIc: bp 163°C (0.5 mm), n_D^{20} 1.5690. IR spectrum (KBr), ν, cm^{-1}: 2970, 1600 (C=C), 1200 (P=O), 1020. ^{1}H NMR spectrum, δ, ppm: 1.53 t (6H, CH_3), 3.08 t (4H, CH_2N), 3.61 t (4H, CH_2O), 3.94 q (4H, CH_2O), 4.18 d.d (1H, CH, $^3J_{HH}$ 14.8, $^2J_{HP}$ 12 Hz), 6.9 t (1H, CH, $^3J_{HH}$ 14.8, $^3J_{HP}$ 14.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.27 (CH_3), 42.9 (CH_2N), 60.88 (CH_2O), 65.97 (CH_2O, morpholine), 75.5 d (CH, $^1J_{PC}$ 201.31 Hz), 153.62 d (=C–N, $^2J_{PC}$ 19.32 Hz). ^{31}P NMR spectrum, δ_P, ppm: 27.59.

Diethyl (*E*)-2-(dimethylamino)prop-1-enephosphonate IId: bp 121°C (0.4 mm), n_D^{20} 1.5680. IR spectrum (KBr), ν, cm^{-1}: 2967, 1554 (C=C), 1209 (P=O), 1018. ^{1}H NMR spectrum, δ, ppm: 1.18 t (6H, CH_3), 2.09 s (3H, CH_3), 2.77 s (6H, CH_3), 3.62 d (1H, CH, $^2J_{HP}$ 9.41 Hz), 3.89 q (4H, CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 15.91 (CH_3), 17.37 d (CH_3, $^3J_{PC}$ 4.23 Hz), 39.29 (CH_3), 60.32 (CH_2O), 73.84 d (CH, $^1J_{PC}$ 215.2 Hz), 160.82 d (=C–N, $^2J_{PC}$ 20.23 Hz). ^{31}P NMR spectrum, δ_P, ppm: 27.22.

Diethyl (*E*)-2-(diethylamino)prop-1-enephosphonate IIe: bp 126°C (0.1 mm), n_D^{20} 1.5699. IR spectrum (KBr), ν, cm^{-1}: 2970, 1558 (C=C), 1213 (P=O), 1029. ^{1}H NMR spectrum, δ, ppm: 0.84 t (6H, CH_3), 1.01 t (6H, CH_3), 1.92 d (3H, CH_3, $^4J_{HP}$ 1.6 Hz), 2.95 q (4H, CH_2N), 3.46 d (1H, CH, $^2J_{HP}$ 9.81 Hz), 3.71 q (4H, CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 12.66 (CH_3), 16.31 (CH_3), 17.15 d (CH_3, $^3J_{PC}$ 5.0 Hz), 43.79 (CH_2N), 60.45 (CH_2O), 72.97 d (CH, $^1J_{PC}$ 217.34 Hz), 158.75 d (=C–N, $^2J_{PC}$ 21.0 Hz). ^{31}P NMR spectrum, δ_P, ppm: 27.46.

Diethyl (*E*)-2-piperidinoprop-1-enephosphonate IIf: bp 170°C (0.5 mm), n_D^{20} 1.5688. IR spectrum (KBr), ν, cm^{-1}: 2970, 1560 (C=C), 1220 (P=O), 1029. ^{1}H NMR spectrum, δ, ppm: 1.1 t (6H, CH_3), 1.38 m (6H, CH_2, piperidine), 1.98 d (3H, CH_3, $^4J_{HP}$ 1.0 Hz), 3.02 t (4H, CH_2N), 3.87 d (1H, CH, $^2J_{HP}$ 9.75 Hz), 3.88 q (4H, CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 15.8 (CH_3), 17.42 d (CH_3, $^3J_{PC}$ 3.57 Hz), 23.65 (*p*-CH_2, piperidine), 24.7 (*m*-CH_2, piperidine), 46.69 (CH_2N), 60.11 (CH_2O), 76.02 d (CH, $^1J_{PC}$ 212.7 Hz), 160.06 d (=C–N, $^2J_{PC}$ 19.33 Hz). ^{31}P NMR spectrum, δ_P, ppm: 27.85.

Diethyl (*E*)-2-morpholinoprop-1-enephosphonate IIg: bp 180°C (0.5 mm), n_D^{20} 1.5700. IR spectrum (KBr), ν, cm^{-1}: 2970, 1560 (C=C), 1213 (P=O), 1024. ^{1}H NMR spectrum, δ, ppm: 1.12 t (6H, CH_3), 2.02 d (3H, CH_3, $^4J_{HP}$ 2.0 Hz), 2.98 t (4H, CH_2N), 3.53 t (4H, CH_2O), 3.8 d (1H, CH, $^2J_{HP}$ 9.0 Hz), 3.85 q (4H, CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 15.8 (CH_3), 16.95 d (CH_3, $^3J_{PC}$ 2.82 Hz), 45.7 (CH_2N), 60.29 (CH_2O), 65.71 (CH_2O, morpholine), 79.19 d (CH, $^1J_{PC}$ 212.9 Hz), 160.64 d (=C–N, $^2J_{PC}$ 19.17 Hz). ^{31}P NMR spectrum, δ_P, ppm: 26.04.

Diethyl (*E*)-2-(diethylamino)but-1-enephosphonate IIh: bp 130°C (0.1 mm), n_D^{20} 1.5671, d_4^{20} 1.0234. IR spectrum (KBr), ν, cm^{-1}: 2970, 1546 (C=C), 1213 (P=O), 1029. ^{1}H NMR spectrum, δ, ppm: 0.90 t (6H, CH_3), 0.93 t (3H, CH_3), 1.07 t (6H, CH_3), 2.4 q (2H, CH_2), 3.0 q (4H, CH_2N), 3.48 d (1H, CH, $^2J_{HP}$ 9.8 Hz), 3.79 q (4H, CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 12.91 (CH_3), 13.96 (CH_3, Et), 16.37 (CH_3), 22.33 d (CH_2, Et, $^3J_{PC}$ 5.1 Hz), 43.3 (CH_2N), 60.45 (CH_2O), 72.54 d (CH, $^1J_{PC}$ 217.33 Hz), 164.43 d (=C–N, $^2J_{PC}$ 21.6 Hz). ^{31}P NMR spectrum, δ_P, ppm: 27.17.

Diethyl (*E*)-2-piperidinobut-1-enephosphonate IIi: bp 156°C (0.25 mm), n_D^{20} 1.5780. IR spectrum (KBr), ν, cm^{-1}: 2973, 1629 (C=C), 1233 (P=O), 1013. ^{1}H NMR spectrum, δ, ppm: 1.21 t (6H, CH_3), 1.25 t (3H, CH_3), 1.5 m (6H, CH_2, piperidine), 2.57 q (2H, CH_2, Et), 3.08 m (4H, CH_2N), 3.85 d (1H, CH, $^2J_{HP}$ 10.3 Hz), 3.93 q (4H, CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 13.02 (CH_3), 16.77 (CH_3), 23.46 d (CH_3, $^3J_{PC}$ 5.18 Hz), 25.14 (CH_2, piperidine), 47.07 (CH_2N), 60.39 (CH_2O), 75.63 d (CH, $^1J_{PC}$ 215.7 Hz), 165.99 d (=C–N, $^2J_{PC}$ 21.72 Hz). ^{31}P NMR spectrum, δ_P, ppm: 27.25.

Diethyl (*E*)-2-(dimethylamino)-2-phenylethenephosphonate IIj: bp 155°C (0.4 mm), n_D^{20} 1.5700. IR spectrum (KBr), ν, cm^{-1}: 2960, 1534 (C=C), 1200 (P=O), 1020. ^{1}H NMR spectrum, δ, ppm: 0.97 t (6H, CH_3), 2.63 s (6H, CH_3), 3.63 q (4H, CH_2O), 4.06 d (1H, CH, $^2J_{HP}$ 9.81 Hz), 7.25 m (5H, arom.). ^{13}C NMR spectrum, δ_C, ppm: 15.73 (CH_3), 39.77 (CH_3), 60.11 (CH_2O), 78.46 d (CH, $^1J_{PC}$ 215.55 Hz), 127.41 (*m*-CH arom.), 128.28 (*p*-CH arom.), 128.56 (*o*-CH arom.), 135.72 d (C_i, arom., $^3J_{PC}$ 7.45 Hz), 163.63 d (=C–N, $^2J_{PC}$ 18.02 Hz). ^{31}P NMR spectrum, δ_P, ppm: 24.06.

Diethyl (*E*)-2-(diethylamino)-2-phenylethenephosphonate IIk: bp 156°C (0.1 mm), n_D^{20} 1.5685,

d_4^{20} 1.0724. IR spectrum (KBr), ν, cm^{-1}: 2970, 1533 (C=C), 1200 (P=O), 1029. ^1H NMR spectrum, δ, ppm: 0.75 m (12H, CH_3), 2.28 q (4H, CH_2N), 3.42 q (4H, CH_2O), 3.87 d (1H, CH, $^2J_{HP}$ 10.3 Hz), 7.0 m (5H, arom.). ^{13}C NMR spectrum, δ_C, ppm: 11.7 (CH_3), 15.16 (CH_3), 42.71 (CH_2N), 59.3 (CH_2O), 76.6 d (CH, $^1J_{PC}$ 217.82 Hz), 126.65–127.54 (*m,p*-CH arom.), 128.15 (*o*-CH arom.), 135.2 d (C_i, arom., $^3J_{PC}$ 5.6 Hz), 161.18 d (=C–N, $^2J_{PC}$ 17.1 Hz). ^{31}P NMR spectrum, δ_P, ppm: 24.14. Mass spectrum (electron impact), *M* 310; *m/z* (I_{rel}, %): 29 (77.9), 72 (51.7), 103 (51.3), 131 (34.4), 174 (100), 282 (29.3), 310 (60.7).

Diethyl (*E*)-2-piperidino-2-phenylethenephosphonate III: bp 160°C (0.1 mm), n_D^{20} 1.5705. IR spectrum (KBr), ν, cm^{-1}: 2970, 1540 (C=C), 1220 (P=O), 1029. ^1H NMR spectrum, δ, ppm: 1.06 t (6H, CH_3), 1.55 m (6H, CH_2, piperidine), 3.0 m (4H, CH_2N), 4.11 q (4H, CH_2O), 4.36 d (1H, CH, $^2J_{HP}$ 9.8 Hz), 7.35 m (5H, arom.). ^{13}C NMR spectrum, δ_C, ppm: 15.82 (*m*-CH_2, piperidine), 15.85 (CH_3), 25.23 (*p*-CH_2, piperidine), 48.62 (*o*-CH_2, piperidine), 60.34 (CH_2O), 81.19 d (CH, $^1J_{PC}$ 214.4 Hz), 127.63 (*m*-CH arom.), 128.33 (*p*-CH arom.), 128.99 (*o*-CH arom.), 136.45 d (C_i, arom., $^3J_{PC}$ 4.07 Hz). ^{31}P NMR spectrum, δ_P, ppm: 24.6.

Diethyl (*E*)-2-morpholino-2-phenylethenephosphonate IIm: bp 165°C (0.1 mm), n_D^{20} 1.5713. IR spectrum (KBr), ν, cm^{-1}: 2970, 1540 (C=C), 1220 (P=O), 1020. ^1H NMR spectrum, δ, ppm: 0.97 t (6H, CH_3), 2.87 t (4H, CH_2N), 3.55 t (4H, CH_2O, morpholine), 3.67 q (4H, CH_2O), 4.37 d (1H, CH, $^2J_{HP}$ 9.2 Hz), 7.27 m (5H, arom.). ^{13}C NMR spectrum, δ_C, ppm: 15.67 (CH_3), 47.59 (CH_2N), 60.38 (CH_2O), 65.94 (CH_2O, morpholine), 83.93 d (CH, $^1J_{PC}$ 212.6 Hz), 127.57 (*m*-CH arom.), 128.75 (*p*-CH arom.), 128.89 (*o*-CH arom.), 135.24 d (C_i, arom., $^3J_{PC}$ 4.07 Hz), 163.77 d (=C–N, $^2J_{PC}$ 16.31 Hz). ^{31}P NMR spectrum, δ_P, ppm: 23.12.

REFERENCES

1. Walker, B.J., *Organophosphorus Reagents in Organic Synthesis,* Cadogan, J.G.G., Ed., London: Academic, 1979, no. 4, pp. 155–206.
2. Altenbach, H.-J. and Korff, R., *Tetrahedron Lett.,* 1981, vol. 22, no. 51, p. 5175.
3. Boeckman, R.K., Walter, M.A., Jr., and Koyano, H., *Tetrahedron Lett.,* 1989, vol. 30, no. 36, p. 4787.
4. Palacios, F., Aparicio, D., and Garcia, J., *Tetrahedron,* 1996, vol. 52, no. 28, p. 9609.
5. Nagata, W. and Hayase, Y., *Tetrahedron Lett.,* 1968, vol. 9, no. 41, p. 4359.
6. Tay, M.K., Aboujaoude, E.E., Collignon, N., and Savignac, P., *Tetrahedron Lett.,* 1987, vol. 28, no. 12, p. 1263.
7. Mohinder, S., Chattha, M.S., and Aguiar, A.M., Jr., *Tetrahedron Lett.,* 1971, vol. 12, no. 18, p. 1419.
8. Palacios, F., Ochoa de Retana, A.M., Oyarzabal, J., and Ezbelete, J.M., *Tetrahedron,* 1998, vol. 54, no. 10, p. 2281.
9. Alikin, A.Yu., Sokolov, M.P., Liorber, B.G., Razumov, A.I., Zykova, T.V., and Zykova, V.V., *Zh. Obshch. Khim.,* 1981, vol. 51, no. 3, p. 547.
10. Alikin, A.Yu., Sokolov, M.P., Liorber, B.G., Razumov, A.I., Zykova, T.V., Zykova, V.V., and Suleimanova, I.N., *Zh. Obshch. Khim.,* 1981, vol. 51, no. 3, p. 556.
11. Palacios, F., Ochoa de Retana, A.M., and Oyarzabal, J., *Tetrahedron Lett.,* 1996, vol. 37, no. 26, p. 4577.
12. Palacios, F., Aparicio, D., and Garcia, J., *Tetrahedron,* 1997, vol. 53, no. 8, p. 2931.
13. Palacios, F., Ochoa de Retana, A.M., and Oyarzabal, J., *Tetrahedron,* 1999, vol. 55, no. 18, p. 5947.
14. Palacios, F. and Ochoa de Retana, A.M., *Tetrahedron,* 1999, vol. 55, no. 10, p. 3091.
15. Lee, S.-L., Hepburn, T.W., Swartz, W.H., Ammon, H.L., Mariano, P.S., and Dunaway-Mariano, D., *J. Am. Chem. Soc.,* 1992, vol. 114, no. 19, p. 7346.
16. Kazankova, M.A., Trostyanskaya, I.G., Lutsenko, S.V., and Beletskaya, I.P., *Tetrahedron Lett.,* 1999, vol. 40, no. 3, p. 559.
17. Saunders, B.C. and Simpson, P., *J. Chem. Soc.,* 1963, p. 3351.
18. Acheson, R.M., Ansel, P.J., and Murray, J.R., *J. Chem. Res. (S),* 1986, p. 378.
19. Pudovik, A.N., Khusainova, N.G., and Ageeva, A.G., *Zh. Obshch. Khim.,* 1964, vol. 34, no. 12, p. 3938.
20. Mohinder, S., Chattha, M.S., and Aguiar, A.M., Jr., *J. Org. Chem.,* 1973, vol. 38, no. 4, p. 820.
21. Maerkl, G. and Merkl, B., *Tetrahedron Lett.,* 1983, vol. 24, no. 52, p. 5865.
22. Portnoy, N.A., Morrow, C.J., Chattha, M.S., Williams, J.C., and Aguiar, A.M., Jr., *Tetrahedron Lett.,* 1971, vol. 12, no. 18, p. 1397.
23. Rousselet, G., Capdeville, P. and Maumy, M., *Tetrahedron Lett.,* 1993, vol. 34, no. 40, p. 6395.
24. Collman, J.P., Hegedus, L.S., Norton, J.R., and Finke, R.G., *Principles and Applications of Organotransition Metal Chemistry,* Mill Valley, CA: Univ. Science Books, 1987. Translated under the title *Metalloorganicheskaya khimiya perekhodnykh metallov,* Moscow: Mir, 1989, book 1, pp. 396–418, 344.
25. Ionin, B.I. and Timofeeva, T.N., *Usp. Khim.,* 1972, vol. 41, no. 4, p. 758.

26. Karplus, M., *J. Chem. Phys.,* 1959, vol. 30, no. 1, p. 11.
27. Duncan, M. and Gallagher, M., *Org. Magn. Reson.,* 1981, vol. 15, p. 37.
28. Timofeeva, T.N., Ignat'ev, V.M., Ionin, B.I., and Petrov, A.A., *Dokl. Akad. Nauk SSSR,* 1969, vol. 189, no. 5, p. 1052.
29. Varlet, J.-M. and Collignon, N., *Synth. Commun.,* 1978, vol. 8, no. 5, p. 335.
30. Varlet, J.-M., and Collignon, N., *Tetrahedron,* 1981, vol. 37, no. 21, p. 3713.
31. Hanessian, S., Hodges, P., Sahao, S.P., and Roy, P.J., *Tetrahedron,* 1986, vol. 27, no. 26, p. 2949.
32. Richard, J.J. and Banks, C.V., *J. Org. Chem.,* 1963, vol. 28, no. 1, p. 123.
33. Kofarski, P. and Soroka, M., *Synthesis,* 1982, no. 3, p. 219.
34. Yudelevich, V.I. and Ionin, B.I., *Fosfororganicheskie lekarstvennye preparaty* (Organophosphorus Drugs), St. Petersburg: Thesa, 1995, pp. 13–14.
35. Tay, M.K., About-Jaudet, E., Collignon, N., and Savignac, P., *Tetrahedron,* 1989, vol. 45, no. 14, p. 4415.
36. Medved', T.Ya., Chmutova, M.K., Nesterova, N.P., Koiro, O.E., Kochetkova, N.E., Myasoedov, B.F., and Kabachnik, M.I., *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1981, no. 9, p. 2121.
37. Matveeva, A.G., Terekhova, M.I., Nesterova, N.P., Petrov, E.S., Matrosov, E.I., and Kabachnik, M.I., *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1988, no. 9, p. 2067.
38. Lomakina, V.I., Mandel'baum, Ya.L., and Mel'nikov, N.N., *Zh. Obshch. Khim.,* 1966, vol. 36, no. 3, p. 447.
39. Mathey, F. and Savignac, P., *Tetrahedron,* 1978, vol. 34, no. 6, p. 649.
40. Landor, P.D., Lander, S.R., and Odyek, O., *J. Chem. Soc., Perkin Trans. 1,* 1977, no. 2, p. 93.
41. Janecki, T. and Bodalski, R., *Tetrahedron,* 1995, vol. 51, no. 6, p. 1721.
42. Pudovik, A.N. and Aladzheva, M.A., *Zh. Obshch. Khim.,* 1963, vol. 33, no. 2, p. 707.
43. Ionin, B.I. and Petrov, A.A., *Zh. Obshch. Khim.,* 1965, vol. 35, no. 11, p. 1917.
44. Dogadina, A.V., Nechaev, Yu.A., Ionin, B.I., and Petrov, A.A., *Zh. Obshch. Khim.,* 1971, vol. 41, no. 8, p. 1662.
45. Zavgorodnii, V.S., Ionin, B.I., and Petrov, A.A., *Zh. Obshch. Khim.,* 1967, vol. 37, no. 4, p. 949.
46. Ionin, B.I., Lebedev, V.B., and Petrov, A.A., *Dokl. Akad. Nauk SSSR,* 1963, vol. 152, no. 6, p. 1354.
47. Anisimov, K.N. and Nesmeyanov, A.N., *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1955, no. 6, p. 1006.