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Acyloxy Derivatives of Trivalent Phosphorus in Amidoalkylation of Hydrophosphoryl Compounds

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Abstract—In order to model the previously suggested mechanism of the P–C bond formation via the Arbuzov reaction, we have studied the interaction of diethylacylphosphite (prepared beforehand as well as generated in situ from tetraethylpyrophosphite) with the in situ generated acyliminium cation. Various conditions of in situ generation of acylphosphite derivatives of P(III) from hydrophosphoryl compounds and acyliminium ions from *N,N*'-alkylidenebiscarbamates have been investigated: solvent nature, acid catalyst, and the reagents mixing order). The results obtained have confirmed the suggested mechanism of three-component reaction of amidoalkylation of hydrophosphoryl compounds with the formation of P–C bond via the Arbuzov reaction of in situ formed intermediates.

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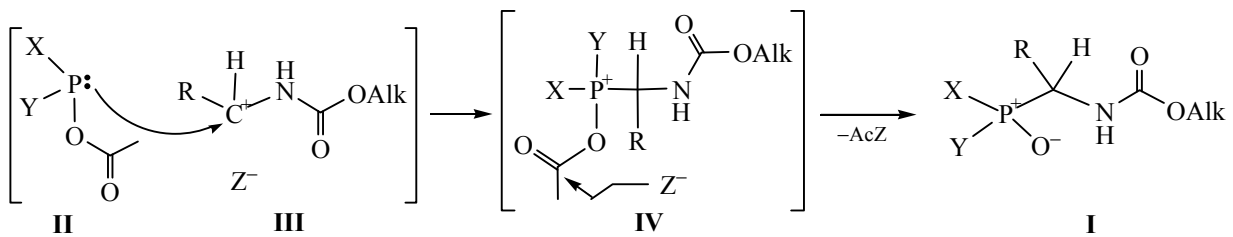
Studies of the synthesis of *N*-alkyloxycarbonyl-α-aminophosphoryl compounds **I** via the three-component reaction of hydrophosphoryl compounds, aldehydes, and alkyl carbamates in acetic anhydride upon cooling suggested a new version of this multi-stage reaction. The mechanism involved the stage of P–C bond formation via the Arbuzov reaction, namely, nucleophilic attack of acetyloxy derivative of trivalent phosphorus **II** at the positively charged carbon atom of iminium cation **III** (Scheme 1). Components **II** and **III** were generated in situ from the starting hydrophosphoryl compound and *N,N*'-alkylidenebis(alkylcarbamate), respectively [1, 2]. The latter was identified as a stable intermediate forming from aldehyde and alkylcarbamate, and was isolated from reaction medium [1, 2]. The subsequent attack of the anion Z at electrophilic carbon atom of POAc fragment of phosphonium intermediate **IV** led to the formation of the target *N*-protected α-aminophosphoryl compound **I** with the elimination of AcZ (Scheme 1) via the Arbuzov reaction [1, 2].

This work was aimed to model the assumed stage of P–C bond formation basing on the previously suggested mechanism [1, 2]. We studied the interaction of the acyloxy derivative of trivalent phosphorus **II** (prepared beforehand) with *N*-alkyloxycarbonyl-iminium cation **III** (generated in situ from *N,N*'-alkylidenebiscarbamate **V** under conditions of acid catalysis) [1–4].

It was found that the interaction of *N,N*'-benzylidenebis(benzylcarbamate) **Va** with diethylacetylphosphite **IIa** in acetic anhydride did not lead to the

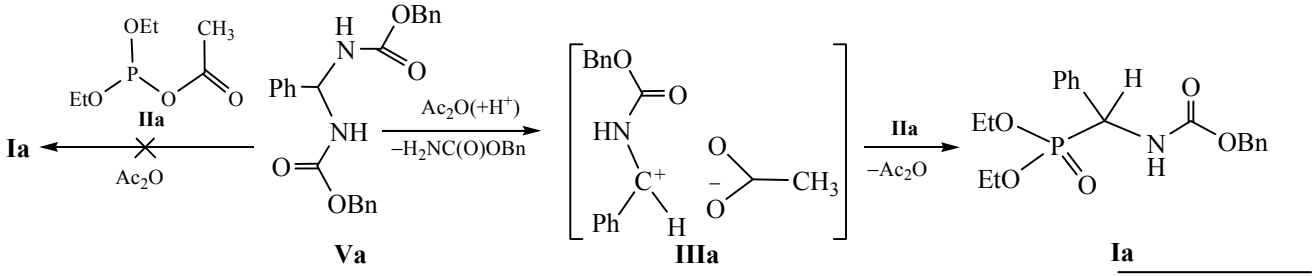
Scheme 1.



Z = Cl, OAc.

formation of the target *N*-benzyloxycarbonyldiethylphosphonate **Ia** (Scheme 2); the reason of that was the absence of acid catalysis required for the in situ generation of the cation **IIIa** from *N,N'*-benzylidenebis(benzylcarbamate) **Va** (Scheme 2). The possible attack of the trivalent phosphorus atom of diethylacetylphosphite **IIa** at the electrophilic carbon atom of benzylidene fragment in **Va** did not result in the target P–C bond formation, in contrast with the successful attack of **IIa** at the positively charged carbon atom of the cation **IIIa** that could only be generated under acid catalysis conditions [1–4].

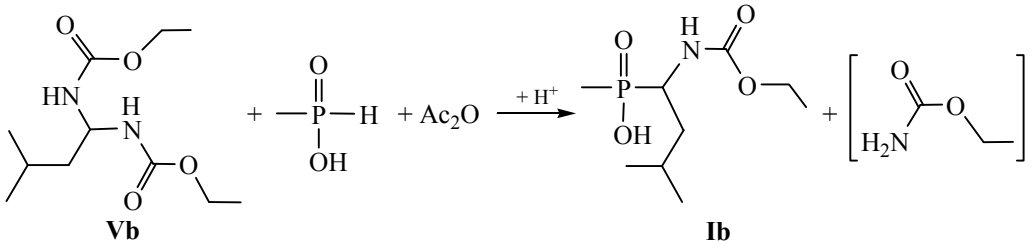
Scheme 2.



The obtained result confirmed our suggestion on the required reaction conditions: not only $P^{III}OAc$ component **II** should have been generated, but also the acid catalysis was necessary for in situ generation of *N*-alkyloxycarbonyliminium cation **III** [1, 2]. Indeed, addition of catalytic amounts of trifluoroacetic acid or *p*-toluenesulfonic acid led to formation of the target product **Ia** in satisfactory yields.

Further, we studied the effect of acid catalysis on the interaction of *N,N'*-isoamylidenebis(ethylcarbamate) **Vb** with methylphosphonous acid in acetic anhydride (Scheme 3) by means of ^{31}P NMR spectroscopy.

Scheme 3.



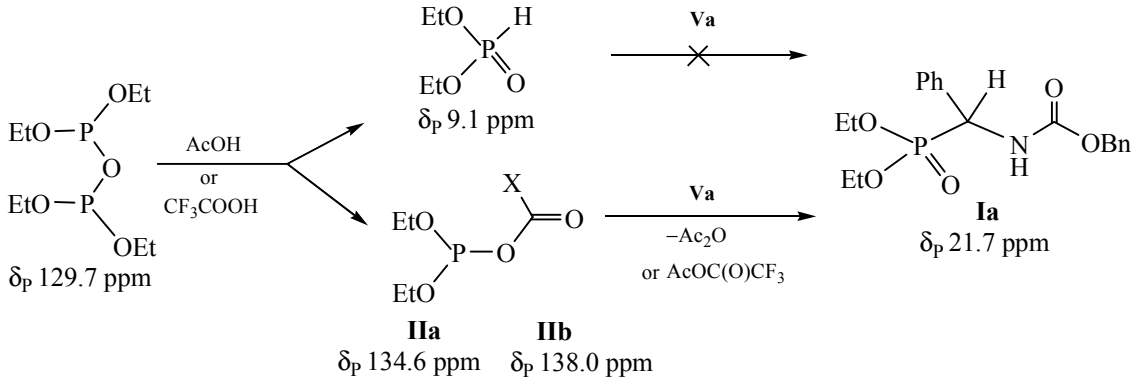
The results confirmed the acid-catalysed mechanism of the reaction, *p*-toluenesulfonic acid (2%) being more efficient catalyst than trifluoroacetic acid (10%) (see figure).

The satisfactory reaction course in acetic anhydride without additionally introduced catalyst could be described as the transformation of hydrophosphoryl compound into acetyloxy derivative of trivalent phosphorus with the formation of acetic acid; the acidity of the latter likely was enough to induce the formation of the corresponding *N*-(alkyloxycarbonyl)iminium cation **III** [1, 2].

Another approach to the reaction mechanism modeling implied using pyrophosphite as the source of trivalent phosphorus acyloxy derivative in situ. Tetraethylpyrophosphite was shown to interact with one equivalent of acetic acid with the formation of diethylacetylphosphite **IIa** and diethylphosphite [5]; we confirmed that by results of ^{31}P NMR spectroscopy in the presence of acetic and trifluoroacetic acids (Scheme 4). Previously, we found that in chloroform, toluene, ethanol, dioxane, tetrahydrofuran, and in acetic acid media the interaction of biscarbamates **V** with hydrophosphoryl compounds did not occur [1, 2].

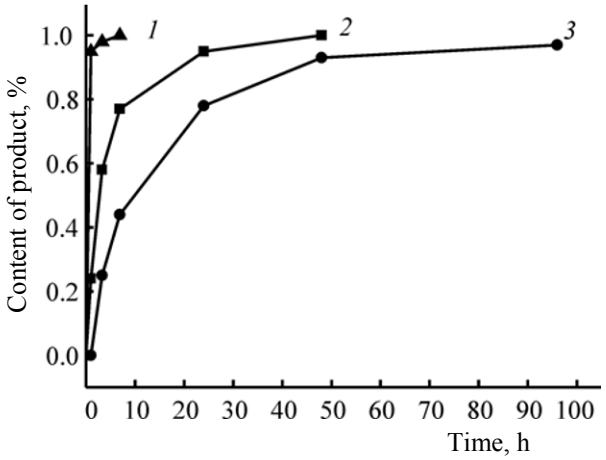
Therefore, in the organic solvent containing an equivalent of acetic acid, pyrophosphite should act as a source of reactive diacetylphsphite **IIa** capable of reacting with acyliminium cation **IIIa**, whereas diethylphosphite in the absence of acetic anhydride should not be reactive under those conditions [1, 2]

Scheme 4.



and should be accumulated unchanged in the reaction medium.

We studied the interaction of tetraethylpyrophosphite with a solution of *N,N'*-benzylidenebis(benzylcarbamate) **Va** in anhydrous chloroform or toluene with varied amount of acetic or trifluoroacetic acid (0.5–1.5 equivalents). The results confirmed the formation of target phosphonate **Ia**; as expected, the second P-containing reaction product was diethylphosphite that was formed from pyrophosphite and was stable under the reaction conditions. However, yield of **Ia** was relatively low, 15% to 23% depending on the nature and amount of the acid catalyst. Furthermore, we observed lower yields of **Ia** in the case when *N,N'*-benzylidenebis(benzylcarbamate) **Va** was in contact with the acid for some period of time before pyrophosphite was added; that was likely due to the instability of the iminium cation **IIIa** in acidic medium.



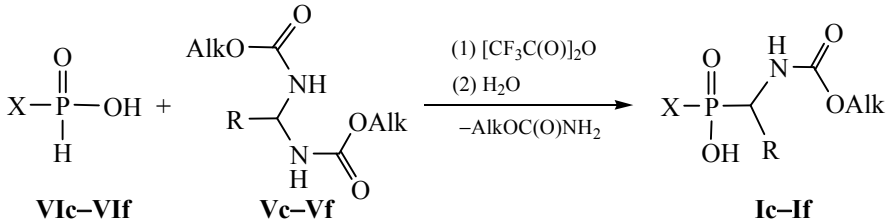
Kinetics of **Ib** accumulation in the reaction mixture (time in h, acetic anhydride medium): (*1*) with *p*-toluenesulfonic acid (2 mol%), (*2*) with trifluoroacetic acid (10 mol %), (*3*) without catalyst. The **Ib** content was calculated as integral intensity of ^{31}P signal of **Ib** with respect to sum of the signals of **Ib** and of methylphosphonous acid.

Therefore, we changed the order of reactants mixing. In particular, we studied the interaction of acid catalyst with a mixture of tetraethylpyrophosphite and biscarbamate **Va** in toluene, methylene chloride, or chloroform, in order to generate **IIa** or IIb and the acyliminium cation simultaneously. That increased the yield of **Ia** to 32–45%, catalysis by CF_3COOH being more efficient. The results confirmed validity of the suggested reaction mechanism, as described above. The particular case of pyrophosphite as a phosphorous-containing component could be generalized to other compounds.

The above-described approach to generate the reactive intermediates by addition of acetic or trifluoroacetic anhydride to a mixture of hydrophosphoryl compound and alkylidenebiscarbamate could be promising in the preparatory syntheses of *N*-protected α-aminophosphoryl compounds. The initial interaction of anhydride with the hydrophsphoryl component **VI** should lead to in situ formation of reactive acyloxy form of trivalent phosphorus **II** and the corresponding acid that would facilitate generation of acyliminium cation **III**.

Addition of trifluoroacetic anhydride to a mixture of *N,N'*-alkylidenebiscarbamate **Vc–Vf** and hydrophosphoryl compound **VIc–VIf** in the methylene chloride of toluene solution upon cooling and subsequent treatment of the mixture with water (Scheme 5) led to reasonably high yields of the target acids **Ic–If** (52–65%) [3, 4].

Scheme 5.



VIc–VIf **Vc–Vf** **Ic–If**

X = R = Me, Alk = Bn (**Ic**); X = EtOC(O)CH_2CH_2, R = *i*-Pr, Alk = Bn (**Id**); R = Ph, Alk = Et (**Ie**);
X = EtOC(O)CH(Me)CH_2, R = Me, Alk = Bn (**If**).

To conclude, this model study confirmed the previously assumed mechanism [1, 2]. of the generation in situ of the acetyloxy derivative of phosphorus(**III**) and of iminium cation (salt) under the conditions of the reaction of amidoalkylation in the acetic anhydride environment followed by their interaction of the type of Arbuzov reaction with the formation of the target P–C bond.

EXPERIMENTAL

^1H, ^{31}P, and ^{13}S NMR spectra were registered on a Brucker spectrometer DPX-200, the references used were TMS (internal) and 85% H_3PO_4 (external). Melting points were determined with Boetius-PHMK or in open capillary.

Thin layer chromatography analysis of the individual compounds and the reaction mixtures was performed using Silufol plates, glass plates (Merck silica gel UV-254 layer of 0.2 mm) [eluent: chloroform–acetone, (4–5):1], or Alufol plates (Kavalier) (neutral aluminum oxide on aluminum foil); the plates were developed in iodine vapor or by UV irradiation. Column chromatography was performed using Silpearl silica gel and L100/160 (Chemapol) or Silica gel 60 (Alfa Aesar).

N,N'-Alkylidenebis(alkylcarbamates) were prepared from the corresponding aldehyde and two equivalents of ethyl or benzyl carbamate in acetic aldehyde [1, 2]. Diethylacetylphosphite was prepared from diethylchlorophosphite and sodium acetate as described in [7]. 2-(Ethoxycarbonyl)propylphosphonous acid and 2-(ethoxycarbonyl)propylphosphonous acid were acid were synthesized by in situ addition of bis(trimethylsilyl)hypophosphite to ethyl acrylate and ethyl methacrylate, respectively, with subsequent alcoholysis of the formed silylphosphonites [8].

Reaction of diethylacetylphosphite with *N,N*'-benzylidenebis(benzylcarbamate). Freslhly distilled diethylacetylphosphite **IIa** (5 mmol) in 5 mL of acetic anhydride was added to a solution of *N,N*'-benzylidenebis(benzylcarbamate) **Va** (5 mmol) in 3 mL of anhydrous chloroform (or methylene chloride); the mixture was stirred during 2 days. TLC and ^{31}P NMR showed that the initial compounds remained practically unchanged [formation of some diethylphosphite (δ_P ~ 12 ppm) and may be acetylphosphonate (δ_P ~ 19 ppm) was detected; in total, no more than 9–11%]. To that solution, trifluoroacetic acid was added (10 mol %), and the mixture was stirred during 20 h. From ^{31}P NMR, the initial **IIa** was completely consumed (signal at ~135 ppm disappeared), and the target product **Ia** was formed (intense phosphonate signal appeared at ~22 ppm). The reaction mixture was evaporated in a vacuum; the residue was dissolved in chloroform (15 mL) and washed with water (3–5 mL). The organic phase was dried over sodium sulfate and evaporated in a vacuum. The residue was crystallized from petroleum ether and recrystallized from ether. Yield 28%, with respect to diethylacetylphosphite.

Upon addition of the catalytic amounts of *p*-toluenesulfonic acid (2 mol %) or trifluoroacetic acid (10 mol %) to a freshly prepared solution of diethylacetylphosphite and *N,N*'-benzylidenebid(benzylcarbamate) in a mixture of acetic anhydride and chloroform or methylene chloride (1:1) yields of **Ia** were 53% (*p*-TsOH) and 37% (CF_3COOH).

Reaction of methylphosphonous acid with *N,N*'-isoamylidenebis(ethylcarbamate) (Vb) in acetic anhydride. The catalyst *p*-TsOH (2 mol %) or CF_3COOH (10 mol %) was added to a freshly prepared solution of *N,N*'-isoamylidenebis(ethylcarbamate) **Vb** (5 mmol) and methylphosphonous acid (5 mmol) in 5 mL of acetic anhydride, or the reaction was performed

without catalyst. The course of the reaction was monitored by ^{31}P NMR; the signals of initial methylphosphonic acid at ~35 ppm and of the forming phosphinic acid at 55 ppm were followed. The change of content of the target product **Ib** with time (h) is given in the figure at different catalysis conditions. Phosphonate **Ib** was isolated from the reaction mixture as described in [2].

Tetraethylpyrophosphite as a source of diethylacetylphosphite in situ**.** *a*. Tetraethylpyrophosphite (4 mmol) in 3 mL of anhydrous toluene was added to a freshly prepared solution of *N,N*'-benzylidenebis (benzylcarbamate) **Va** (4 mmol) in 3 mL of anhydrous chloroform containing acetic or trifluoroacetic acid (0.5–1.5 equivalent); the solution was stirred at room temperature. The course of the reaction was monitored by ^{31}P NMR. The reaction mixture was diluted with 10–15 mL of toluene, and then evaporated in a vacuum. The semicrystalline precipitate was partitioned between sodium carbonate saturated aqueous solution (15 mL) and ether (15 mL). Benzyl carbamate from the solution was filtered off, aqueous part of the filtrate was acidified to pH ~ 6–7 and extracted with chloroform (3×10 mL). The combined organic extract was dried over magnesium sulfate and evaporated in a vacuum. The residue was subjected to chromatography on silica gel ($CHCl_3$:*i*-PrOH, 20:1). Phosphonate **Ia** was crystallized from petroleum ether and recrystallized from ether. Yield from 15% (catalysis with 1.5 eq. of AsOH) to 23% (1.0 eq. of CF_3COOH) with respect to pyrophosphite. The phosphonate yield was significantly decreased when tetraethylpyrophosphite was added long time after the acid catalyst mixing with biscarbamate.

b. Upon cooling, acetic or trifluoroacetic acid (4–6 mmol) was slowly dropwise added to a solution of the mixture of tetraethylpyrophosphite (4 mmol) and *N,N*'-benzylidenebis(benzylcarbamate) **Va** (4 mmol) in 5–6 mL of anhydrous methylene chloride, chloroform, or toluene. The formed solution was stirred at room temperature, the course of the reaction was monitored with ^{31}P NMR. Subsequently, the mixture was treated as discussed above. The target product yield was 32–45% with respect to pyrophosphite. CF_3COOH was more efficient as catalyst.

Acetic and trifluoroacetic anhydrides in generating reactive intermediates. Upon cooling, acetic or trifluoroacetic anhydride (3 mmol) was slowly dropwise added to a mixture of *N,N*'-alkylidenebiscarbamate **Vc–Vf** (3 mmol) and the corresponding hypophosphorus acid **VIc–VIf** (3 mmol) in toluene or methylene chloride (5 mL). The reaction mixture was stirred during 10–48 h at room temperature, the course of the reaction was monitored by ^{31}P NMR. The semicrystalline residue (after evaporation of the reaction mixture) was partitioned between saturated aqueous solution of sodium carbonate (15 mL) and ether (15 mL). Alkylcarbamate from the solution was filtered off; the aqueous part of the filtrate was acidified to pH 1~2 and extracted with chloroform (3×10 mL). The organic phase was dried over magnesium sulfate and then subjected to chromatography on silica gel ($CHCl_3$:*i*-PrOH:AcOH = 95:4:1) to obtain the corresponding *N*-protected α-aminophosphinic acids (**Id**, **If**) in the form of white crystals. In some cases, the residue crystallized spontaneously or after treatment with ether or petroleum ether, and the target compounds were isolated after additional crystallizeation from ether without chromatography (**Ic**, **Ie**). Yields of the products were 52–65% with trifluoroacetic anhydride; the of use of acetic anhydride decreased the yields to 23–31%. The evaporation of the hypophosphorus acid with acetic anhydride without heating before introducing it to the reaction mixture was found to increase the yields of **I**.

Diethyl ether of α-(*N*-benzyloxycarbonyl)aminobenzylphosphonic acid (Ia), mp 110–111°C (ether) (mp 113–114°C [6]), R_f ~ 0.70 [$CHCl_3$:$CO(CH_3)_2$ = 4:1]. ^{1}H NMR spectrum (CCl_4 + CD_3OD), δ, ppm: 1.23 d.t (6H, $\underline{CH}_3SH_2$, $^4J_{PH}$ 2.0 Hz), 4.03–4.23 m (4H, $OS\underline{H}_2CH_3$), 5.04–5.26 m (2H, $OS\underline{H}_2Ph$), 6.26 br.s (1H, CH), 7.50–7.70 m (10H, 2Ph). ^{31}P NMR spectrum ($CDCl_3$): δ_P 22.1 ppm.

1-(Ethyloxycarbonylamino)-3-methylbutylphosphinic acid (Ib), mp 143–144°C (ether) (mp 144–146°C [1]), R_f ~ 0.10 [$CHCl_3$:$CO(CH_3)_2$ = 4:1]. ^{1}H NMR spectrum (CCl_4 + CD_3OD), δ, ppm: 0.93 d (3H, J_{HH} 6.6 Hz), 0.97 d (3H, J_{HH} 6.6 Hz), 1.26 t (3H, CH_3), 1.38 d (3H, CH_3, J_{PH} 14.1 Hz), 1.40–1.55 m (2H, CH_2), 1.60–1.85 m (1H, CH), 3.74–3.88 m (1H, CH), 4.08 q (2H, CH_2, $^3J_{HH}$ 7.0 Hz). ^{31}P NMR spectrum (CCl_4 + CD_3OD, 5:1): δ_P 52.2 ppm.

1-(Benzyloxycarbonylamino)ethylmethylphosphinic acid (Ic), mp 121–122°C (ether) (mp 100–101°C [2]), R_f ~ 0.15 [$CHCl_3$:$CO(CH_3)_2$ = 4:1]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.35 d.d (3H, $\underline{CH}_3CH$, $^3J_{HH}$ 7.1, $^3J_{PH}$ 15.0 Hz), 1.45 d (3H, CH_3P, $^2J_{PH}$ 15.4 Hz), 3.85–4.10 m (1H, SHN), 4.90–5.15 m (2H, CH_2Ph),

5.40 d (1H, NH, $^3J_{HH}$ 9.7 Hz), 7.23–7.38 m (5H, Ph), 10.60 br.s (1H, POOH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 12.4 d ($^1J_{PC}$ 93.3 Hz), 13.9, 46.0 d ($^1J_{PC}$ 1 07.6 Hz), 67.2, 128.1, 128.2, 128.5, 136.1, 155.9 d ($^3J_{PC}$ 5.1 Hz). ^{31}P NMR spectrum ($CDCl_3$): δ_P 54.9 ppm. ^{31}P NMR spectrum (DMSO-d_6), δ_P 47.1 ppm.

1-(Benzyloxycarbonylamino)-2-methylpropyl-2-(ethyloxycarbonyl)ethylphosphinic acid (Id), mp 86–88°C (ether), R_f 0.15 [$CHCl_3$:$CO(CH_3)_2$ = 4:1]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.98 d (3H, CH<u>CH</u>$_3$, $^3J_{HH}$ 6.6 Hz), 1.02 d (3H, CH<u>CH</u>$_3$, $^3J_{HH}$ 5.3 Hz), 1.23 t (3H, CH_3), 1.88–2.08 m (2H, CH_2), 2.22–2.34 m (1H, CH), 2.51–2.62 m (2H, CH_2), 3.89 d.d.d (1H, CHN, $^3J_{HH}$ 4.0, $^3J_{HH}$ 10.6, $^2J_{PH}$ 10.1 Hz), 4.12 q (2H, CH_2O, $^3J_{HH}$ 7.0 Hz), 5.12 br.s (2H, PhC<u>H</u>$_2$O), 5.26 d (1H, NH, $^3J_{HH}$ 10.6 Hz), 7.25–7.40 m (5H, Ph), 10.88 br.s (1H, POOH). ^{1}H NMR spectrum (CD_3OD), δ, ppm: 1.00 d (3H, CH<u>CH</u>$_3$, $^3J_{HH}$ 4.7 Hz), 1.03 d (3H, CH<u>CH</u>$_3$, $^3J_{HH}$ 3.3 Hz), 1.23 t (3H, CH_3, $^3J_{HH}$ 7.0 Hz), 1.92–2.03 m (2H, CH_2), 2.15–2.28 m (1H, CH), 2.44–2.60 m (2H, CH_2), 3.79 d.d (1H, CHN, $^3J_{HH}$ 5.1, $^2J_{PH}$ 10.2 Hz), 4.12 q (2H, CH_2O, $^3J_{HH}$ 7.0 Hz), 5.08–5.17 m (2H, PhC<u>H</u>$_2$O), 7.25–7.40 m (5H, Ph). ^{13}C NMR spectrum (CD_3OD), δ, ppm: 14.5, 18.8 d ($^3J_{PC}$ 5.1 Hz), 21.2 d ($^3J_{PC}$ 9.1 Hz), 23.8 d ($^1J_{PC}$ 91.5 Hz), 27.5 d ($^2J_{PC}$ 2.6 Hz), 29.2 d ($^2J_{PC}$ 1.5 Hz), 56.1 d ($^1J_{PC}$ 106.1 Hz), 62.0, 67.9, 128.8, 129.0, 129.5, 138.2, 159.0 d ($^3J_{PC}$ 5.5 Hz), 173.8 d ($^3J_{PC}$ 15.7 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_C, ppm: 55.2, 53.9 (~13%) [4]. Found, %: C 55.03, 55.13; H 7.13, 7.20; P 8.39, 8.34. $C_{17}H_{26}NO_6P$. Calculated, %: C 54.98; H 7.06; P 8.34.

α-(Ethyloxycarbonylamino)benzyl-2-(ethyloxycarbonyl)ethylphosphinic acid (Ie), mp 147–148°C (ether), R_f 0.15 [$CHCl_3$:$CO(CH_3)_2$ = 4:1]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.21 t (3H, CH_3, $^3J_{HH}$ 7.1 Hz), 1.25 t (3H, CH_3, $^3J_{HH}$ 7.1 Hz), 1.55–2.00 m (2H, CH_2), 2.30–2.45 m (2H, CH_2), 4.10 q (2H, CH_2, $^3J_{HH}$ 7.0 Hz), 4.14 q (2H, CH_2, $^3J_{HH}$ 7.0 Hz), 5.02 d.d (1H, PCH, $^3J_{HH}$ 10.0, $^3J_{PH}$ 10.0 Hz), 5.90–6.05 m (1H, NH), 7.14 br.s (1H, POOH), 7.18–7.33 m (5H, Ph). ^{1}H NMR spectrum (CCl_4 + CD_3OD, 5:1), δ, ppm: 1.26 t (3H, CH_3, $^3J_{HH}$ 7.0 Hz), 1.29 t (3H, CH_3, $^3J_{HH}$ 7.0 Hz), 1.78–2.06 m (2H, CH_2), 2.39–2.60 m (2H, CH_2), 4.00–4.23 q (4H, $2CH_2$, $^3J_{HH}$ 7.0 Hz), 4.97 d (1H, CH, $^2J_{PH}$ 13.7 Hz), 7.20–7.45 m (5H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.1, 14.6, 21.7 d ($^1J_{PC}$ 91.6 Hz), 26.3 d ($^2J_{PC}$ 2.9 Hz), 54.1 d ($^1J_{PC}$ 99.6 Hz), 60.3, 60.4, 127.2, 127.3, 128.0, 128.2, 136.3, 156.3 d ($^3J_{PC}$ 7.9 Hz), 172.1 d ($^3J_{PC}$ 15.9 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 52.3, 51.0 [4]. ^{31}P NMR spectrum (CCl_4 + CD_3OD, 5:1): δ_P 46.1 ppm. MS spectrum, *m*/*z* (I_{rel}, %): 344 (3.4) $[M + H]^+$, 178 (100) $PhC^+HNHC(O)OCH_2CH_3$, 165 (44) $EtO(O)CCH_2CH_2P^+H(O)OH$. Found, %: C 52.54, 52.61; H 6.39, 6.41; N 4.11, 4.11. $C_{15}H_{22}NO_6P$. Calculated, %: C 52.48; H 6.46; N 4.08.

1-(Benzyloxycarbonylamino)-ethyl-2-(ethyloxycarbonyl)propylphosphinic acid (If), mp 117–118°C (ether), R_f 0.13 [$CHCl_3$:$CO(CH_3)_2$ = 4:1]. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.22 t (3H, CH_3, $^3J_{HH}$ 7.0 Hz), 1.24 d (3H, CH_3, $^3J_{HH}$ 7.0 Hz), 1.34 d.d (3H, <u>CH</u>$_3$CH, $^3J_{HH}$ 7.5, $^3J_{PH}$ 14.9 Hz), 1.65–1.85 m (1H, CH_2P), 2.15–2.35 m (1H, CH_2P), 2.58–2.97 m [1H, CHC(O)], 3.95–4.15 m (1H, CHN), 4.11 q (2H, CH_2O, $^3J_{HH}$ 7.0 Hz), 5.11 br.s (2H, OC<u>H</u>$_2$Ph), 5.38 d (1H, NH, $^3J_{HH}$ 7.5 Hz), 7.20–7.45 m (5H, Ph), 9.72 br.s (1H, POOH). ^{1}H NMR spectrum (CCl_4:DMSO-d_6 = 3:1), δ, ppm: 1.12–1.17 m [6H, <u>CH</u>$_3$CH$_2$ + <u>CH</u>$_3$CHC(O)], 1.19 d.d (3H, <u>CH</u>$_3$CH, $^3J_{HH}$ 7.5, $^3J_{PH}$ 10.6 Hz), 1.51–1.68 m (1H, CH_2P), 1.91–2.08 m (1H, CH_2P), 2.57–2.77 m [1H, CHC(O)], 3.58–3.83 m (1H, CHN), 3.87–4.13 m (2H, CH_2O), 4.93– 5.08 m (OC<u>H</u>$_2$Ph), 7.23–7.42 m (5H, Ph), 7.53 d (1H, NH, $^3J_{HH}$ 8.8 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 13.8, 14.0, 18.6 d ($^2J_{PC}$ 7.0 Hz), 18.8* d ($^2J_{PC}$ 8.1 Hz) (hereinafter asterisk marks the diastereomers signals), 29.3 d ($^1J_{PC}$ 88.6 Hz), 29.4* d ($^1J_{PC}$ 88.2 Hz), 33.4, 45.7 d ($^1J_{PC}$ 105.8 Hz), 46.0* d ($^1J_{PC}$ 105.8 Hz), 60.1, 65.6, 127.7, 127.8, 128.4, 137.1, 155.8 d ($^3J_{PC}$ 3.7 Hz), 175.1 d ($^3J_{PC}$ 9.5 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 55.0, 53.6 [4]. Found, %: C 53.57, 53.49; H 6.92, 6.87; P 8.37, 8.43. $C_{16}H_{24}NO_6P$. Calculated, %: C 53.78; H 6.77; P 8.67.

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