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Synthesis and Some Transformations of Dimethyl Anabasylethynephosphonate

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Abstract—A new phosphorylated ynamine, dimethyl anabasylethynephosphonate, was synthesized by reaction of dimethyl chloroacetylenephosphonate with anabasine. Anabasylethynephosphonate obtained was shown to react under mild conditions with primary aromatic amines like *p*-chloroaniline, *p*-anisidine, and *p*-aminoacetophenone, whose pK_b values are in the range of 9–13, to form new asymmetrical phosphorylated acetamidines in high yields. Structure of the compounds obtained was proved by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy.

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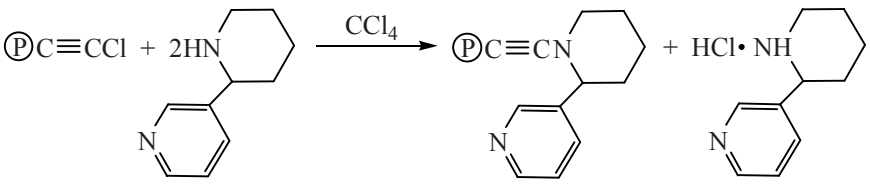
Anabasine belongs to biheterocyclic amines, and is the main alkaloid of *Anabasis aphilla* plants. Owing to the presence of pyridine and pyperidine fragments in its structure anabasine is a precursor for the synthesis of practically important biologically active compounds containing various functions enhancing their biological active properties [1, 2]. Alkaloid anabasine belongs to ganglionary toxins by its pharmacological properties and is a typical H-cholinomimetic agent [3]. It was shown [4] that the substitution of a hydrogen atom at the pyperidine ring nitrogen atom decreased the toxicity of the substance, and some interesting biological properties appeared.

Aiming at the creation of the new phosphorus-containing anabasine derivatives, we synthesized anabasylethynephosphonate and studied some of its transformations. Synthesis of dimethyl anabasylethynephosphonate was carried out by analogy with the procedure described earlier [5], from chloroacetylenephosphonate and anabasine. The reaction was performed in the medium of anhydrous carbon tetrachloride using the starting chloride and amine in molar amounts 1:2.

The reaction progress was monitored by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy and also by the ^{1}H–{^{31}P} double magnetic resonance. Thus, 2 h after mixing the reagents a signal at δ_P 0 ppm was registered in the ^{1}H–{^{31}P} NMDR spectrum. Its chemical shift coincided with that of the phosphorus atom in the spectra of phosphorylated ynamines. In the ^{31}P NMR spectrum intensity of signal at δ_P –8.6 (^{31}P resonance of the initial chloroacetylenephosphonate) decreases to full disappearance, whereas the intensity of signal at δ_P 0 ppm belonging to the product of chlorine substitution increases.



I

Ⓟ = P(O)(OMe)$_2$.

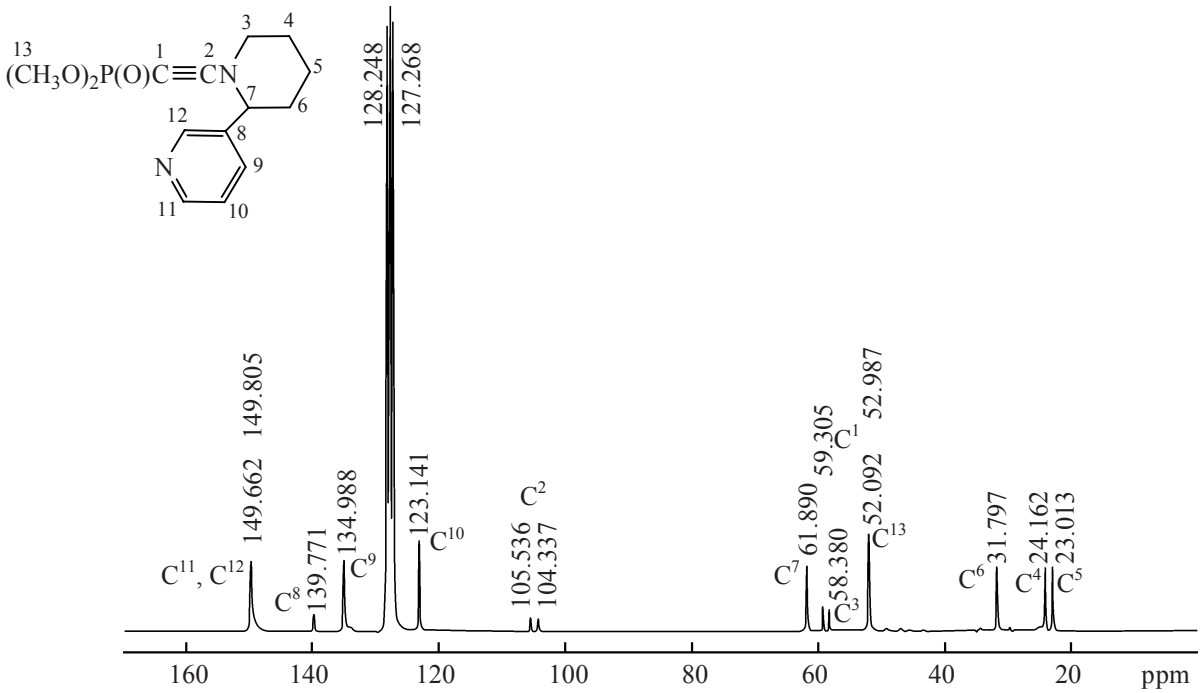
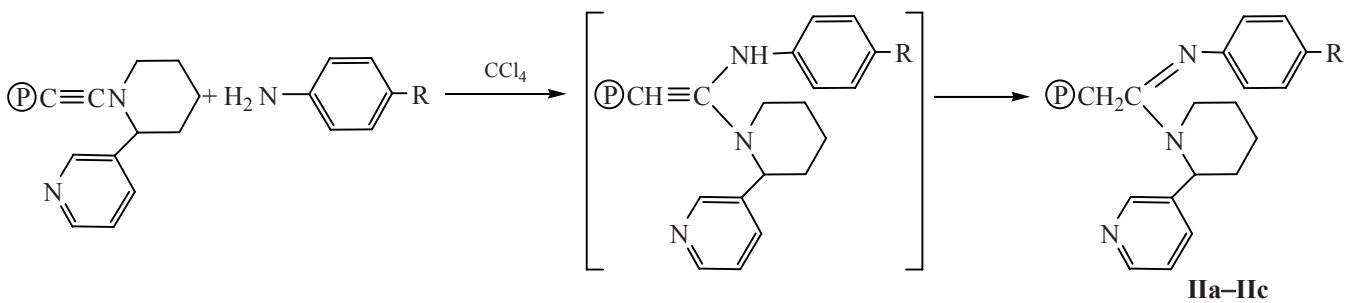


Fig. 1. ^{13}C NMR spectrum of dimethyl anabasylethynephosphonate (**I**).

Structure of dimethyl anabasylethynephosphonate obtained was proved by the ^{1}H, ^{13}C and ^{31}P NMR data. Thus, in the ^{13}C spectrum (Fig. 1) two doublet signals were observed characteristic of the triple bond carbon atoms. The signal of carbon atoms connected directly with the phosphorus atom appeared in the region of δ_C 55.33 ppm with a large spin–spin coupling constants with the phosphorus nucleus $^{1}J_{CP}$ 328.4 Hz. The triple bond carbon atoms bound to the anabasine fragment were registered downfield at δ_C 103.51 ppm with the coupling constant to the phosphorus atom $^{2}J_{CP}$ 62.21 Hz. The methoxy group carbon atoms gave rise to a doublet signal at δ_C 51.05 ppm with the coupling constant $^{2}J_{CP}$ 5.2 Hz. As would be expected, the chemical shift of phosphorus atom in the anabasylethynephosphonate was close to zero. These data are well consistent with the spectral characteristics of the known phosphorylated ynamines [5, 6].

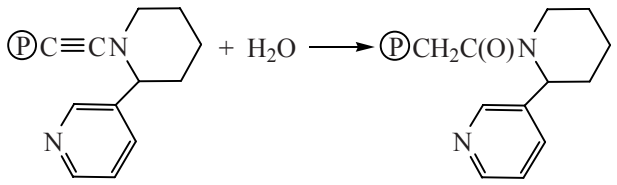
It is known that aminoethynephosphonates are capable to add aromatic amines at the triple bond to form asymmetrical acetamidines [8]. In the course of our study of the reaction between dimethyl anabasylethynephosphonate and aromatic amines (pK_b 9–13) it was shown to occur very smoothly, chemo- and regioselectively to form asymmetrical phosphorylated acetamidines in high yields. The reaction proceeded at heating initial reagents to 60–70ºC for 0.5–1 h without catalysts. The reaction probably occurs through the stage of endiamines formation followed by rapid rearrangement into the corresponding amidine:



Ⓟ = $P(O)(OMe)_2$; R = Cl, CH_3O, CH_3CO.

The phosphorylated acetamidines are colored viscous liquids with faint odor. The ^{1}H, ^{13}C and ^{31}P NMR data confirm that phosphorylated acetamidines are formed in the reaction of dimethyl anabasylethynephosphonate with aromatic amines. Thus, in the ^{1}H NMR spectra of acetamidines obtained the magnetically nonequivalent methylene protons of CH_2P-fragment give rise to two characteristic doublet signals in the region of 3.0–3.2 ppm with spin-spin coupling constants with phosphorus nucleus $^{2}J_{HP}$ 21–22 Hz. In the ^{13}C NMR spectrum there are two doublet signals: an intense signal at δ_C 24–26 ppm with a large coupling constants $^{1}J_{CP}$ 135 Hz belonging to the resonance of carbon atoms directly bound to the phosphorus atom and a low-intensity signal downfield at δ_C 149–151 ppm with coupling constants with the phosphorus nucleus $^{2}J_{CP}$ 6–7 Hz originating from the resonance of the carbon atom connected to two nitrogen-containing groups. The chemical shift values of the phosphorus atom in phosphorylated acetamidines are in the range of +22 to +23 ppm.

We emphasize that the initial dimethyl anabasylethynephosphonate, like the other aminoethynephosphonates reacts readily with even trace amounts of water and air moisture transforming into the corresponding phosphonoacetic acid amide.



III

Ⓟ = $P(O)(OMe)_2$.

This side reaction is extremely undesirable since it is difficult to separate the target product, phosphorylated acetamidine, from the compound of amide structure. Therefore, at high air moisture it is essential to use the protective atmosphere of dry inert gases (for example, argon) in addition to the application of anhydrous solvent and the carefully dried chemical glassware for the synthesis of phosphorylated acetamidines.

Structure of the compounds obtained was confirmed by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. Thus, in the ^{1}H NMR spectrum of anabasyl-*N*-(4-chlorophenyl)dimethoxyphosphorylacetamidine **IIa** we observed a multiplet of piperidine fragment protons in the strong field at δ_H 1.48–1.70 ppm. Doublet signals of the nonequivalent protons of CH_2P-group are registered in the region of 3.11 and 3.15 ppm with coupling constants to the phosphorus nucleus $^{2}J_{HP}$ 22.2 Hz. Protons of CH_3O-groups give two doublet signals at δ_H 3.61 and 3.66 ppm ($^{3}J_{HP}$ 11.8 Hz). Two doublet signals at δ_H 3.75 ($^{2}J_{HH}$ 11.0 Hz) and 3.81 ppm ($^{2}J_{HH}$ 11.0 Hz) belong to CH_2N-fragment protons of piperidine ring. The piperidine CHN-fragment proton is registered as a poorly resolved multiplet at δ_H 5.93 ppm. In the weak field *ortho*- and *meta*-protons of aromatic ring give two doublet signals as *AB*-system. A signal at δ_H 6.65 ppm belongs to the protons in the *ortho*-position to the nitrogen atom involved into the amidine group, with spin-spin coupling constants to adjacent *meta*-protons $^{3}J_{HH}$ 8.6 Hz. *meta*-Protons are registered as a second part of *AB*-system in the region of δ_H 7.17 ppm ($^{3}J_{HH}$ 8.6 Hz). In addition, the spectrum contains signals of anabasine pyridine fragment in weak field at δ_H 7.28 (multiplet, α-CH), 7.64 (doublet, γ-CH, $^{3}J_{HH}$ 7.2 Hz), 8.46 (doublet, α-CH, $^{3}J_{HH}$ 4.4, 7.2 Hz) and 8.54 ppm (singlet, β-CH).

In the ^{13}C NMR spectrum of compound **IIa** (Fig. 2) we observed signals of piperidine carbon atoms in the most strong field at δ_C 19.38 (γ-CH_2), 25.62 and 27.39 (β-CH_2), 42.71 (α-CH_2), 51.97 (α-CH) ppm. A doublet signal of the carbon atom directly connected to the phosphorus is registered at δ_C 25.12 ppm with a coupling constants $^{1}J_{CP}$ 135.3 Hz. The carbon atoms of CH_3O-groups give doublet signal at δ_C 52.76 ppm ($^{2}J_{CP}$ 7.9 Hz).

Signals of carbon atoms of benzene ring and pyridine fragments are shifted downfield. The phenyl carbon atoms in the *ortho*-position to the amidine group nitrogen are registered in the region of δ_C 123.32 ppm. In the weaker field there is a signal of similar intensity at δ_C 128.70 ppm belonging to the aromatic ring *meta*-carbon atoms. The aromatic carbon atom connected to the chlorine atom gives a weak signal at δ_C 148.30 ppm; the signal at δ_C 135.3 ppm belongs to the *ipso*-carbon atom. Singlet signals of the carbon atoms of pyridine fragment are registered at δ_C 123.42 (β-CH), 134.95 (γ-CH), 147.26 (β-C), 149.01 (α-CH_2) ppm. A doublet signal in the region of δ_C 150.95 ppm originated from C=N fragment carbon atom with a low spin-spin coupling constant with the phosphorus nucleus $^{2}J_{CP}$ 7.1 Hz. Chemical shift of phosphorus in anabasyl-*N*-(4-chlorophenyl)dimethoxyphosphorylacetamidine **IIa** is +23.27 ppm characteristic of the tetracoordinated phosphorus atom bound to the sp^3-hybridized carbon atom.

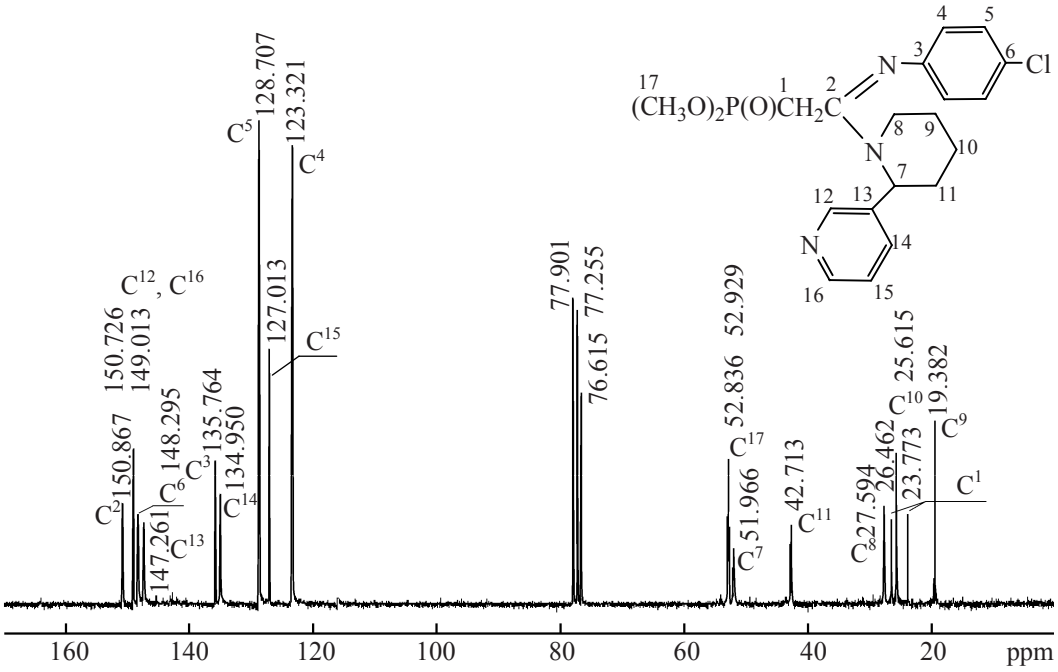


Fig. 2. ^{13}C NMR spectrum of anabasyl-*N*-(4-chlorophenyl)dimethoxy-phosphorylacetamidine (**IIa**).

Thus, it was established that the reaction of dimethyl anabasylethynephosphonate with primary aromatic amines like *p*-chloroaniline, *p*-anisidine, and *p*-aminoacetophenone (pK_b 9–13) proceeded under mild conditions to form the new asymmetrical phosphorylated acetamidines in high yields.

Study of the biological activity of compounds containing amidine function has received much attention in the literature. The presence of phosphonate moiety in combination with the nitrogen-containing fragment of amidine type suggests the appearance of biological activity in these compounds, what is confirmed in some cases [8, 9]. It is presumable that the incorporation of an anabasine moiety into the molecule of these compounds would modify their biological activity. We performed a nonexperimental screening of biological activities for compounds obtained which suggests that the anabasine-containing derivatives of phosphorylated acetamidines **IIa–IIc** may possess moderate antihypertensive, nootropic, antineurotic, miotic, antihypoxic, insecticidal, and antitumor actions. The calculating prediction was carried out on the Orekhovich State University site using PASS program package [10].

EXPERIMENTAL

The used organic solvents and reactants were purified and dried by the standard procedures. The ^1H, ^{13}C, and ^{31}P NMR spectra were registered on Bruker C-400 (^1H, 400 MHz) and Bruker C-200 (^{13}C, 50.328 MHz, and ^{31}P, 81.014 MHz) spectrometers using $CDCl_3$ as a solvent. The chemical shifts are given relative to TMS (^1H, ^{13}C). The ^{31}P NMR spectra were recorded relative to external 85% phosphoric acid. The $^1H–\{^{31}P\}$ NMR spectra were measured on a Tesla BS-497 device (100 MHz).

Dimethyl anabasylethynephosphonate (I). To a solution of 1.94 g (0.012 mol) of anabasine in 5 ml of anhydrous carbon tetrachloride was dropwise added 1 g (0.006 mol) of dimethyl chloroacetylenephosphonate under vigorous stirring and cooling to 0–5°C. Then the reaction mixture was kept for 1 h at room temperature. The precipitated anabasine hydrochloride salt was filtered off on a glass frit. The solvent was removed under a water-jet pump vacuum. Yield 1.23 g (70%).

^1H NMR spectrum, δ_H, ppm ($CDCl_3$): 1.27 m (6H, β,β,γ-$CH_{2pyperid.}$), 2.68 m (1H, α-$CH_{2pyperid.}$), 3.02 d

(1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 11.4 Hz), 3.32 d (3H, CH_3O, $^3J_{HP}$ 12.2 Hz), 3.33 d (3H, CH_3O, $^3J_{HP}$ 12.2 Hz), 3.55 m (1H, α-$CH_{pyperid.}$), 6.91 m (1H, β-$CH_{pyrid.}$, $^3J_{HH}$ 2.4, 7.8 Hz), 7.34 d (1H, γ-$CH_{pyrid.}$, $^3J_{HH}$ 7.8 Hz), 8.47 d (1H, α-$CH_{pyrid.}$, $^3J_{HH}$ 2.4 Hz), 8.58 s (1H, α-$CH_{pyrid.}$). ^{13}C NMR spectrum, δ_C, ppm ($CDCl_3$): 22.80 (γ-$CH_{2pyperid.}$), 23.85 (β-$CH_{2pyperid.}$), 31.59 (β-$CH_{2pyperid.}$), 51.05 d (CH_3O, $^2J_{CP}$ 5.2 Hz), 55.33 d (CP, $^1J_{CP}$ 328.4 Hz), 57.55 (α-$CH_{pyperid.}$), 61.61 (α-$CH_{2pyperid.}$), 103.51 d (≡CN, $^2J_{CP}$ 62.21 Hz), 122.27 (β-$CH_{pyrid.}$), 134.23 (γ-$CH_{pyrid.}$), 139.65 (β-$C_{pyrid.}$), 147.62 (α-$CH_{pyrid.}$), 148.64 (α-$CH_{pyrid.}$). ^{31}P NMR spectrum, δ_P, ppm ($CDCl_3$): 0.07.

General procedure of anabasyl-*N*-phenyldimethoxyphosphorylacetamidines synthesis. To a solution of dimethyl anabasylethynephosphonate in anhydrous carbon tetrachloride was added equimolar amount of primary aromatic amine, whereupon the reaction mixture was refluxed for 0.5–1 h avoiding the air moisture. The solvent was evaporated under a water-jet pump vacuum; the residue was a viscous colored liquid. The crude product yields were quantitative. Since the chromatography of little amounts of organophosphorus compounds is a labor-consuming process and requires great amounts of solvents the acetamidines obtained were not subjected to chromatographic purification.

The phosphorylated acetamidines are sufficiently stable to the air moisture, therefore, notwithstanding the fact that their syntheses should be carried out with atmost care owing to high tendency of the initial aminoethynephosphonates to react with water, the following analysis and isolation of compounds obtained does not require special conditions.

Anabasyl-*N*-(4-chlorophenyl)dimethoxyphosphorylacetamidine (IIa) was prepared similarly from 1.23 g (0.0042 mol) of dimethyl anabasylethynephosphonate and 0.53 g (0.0042 mol) of *p*-chloroaniline. ^1H NMR spectrum, δ_H, ppm ($CDCl_3$): 1.48–1.70 m (6H, β,β,γ-$CH_{2pyperid.}$), 3.11 d (1H, CH_2P, $^2J_{HP}$ 22.2 Hz), 3.15 d (1H, CH_2P, $^2J_{HP}$ 22.2 Hz), 3.61 d (3H, CH_3O, $^3J_{HP}$ 11.8 Hz), 3.66 d (3H, CH_3O, $^3J_{HP}$ 11.8 Hz), 3.75 d (1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 11.0 Hz), 3.81 d (1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 11.0 Hz), 5.93 m (1H, α-$CH_{pyperid.}$), 6.65 d (2H, =NC$CH_{arom.}$, $^3J_{HH}$ 8.6 Hz), 7.17 d (2H, ClC$CH_{arom.}$, $^3J_{HH}$ 8.6 Hz), 7.28 m (1H, β-$CH_{pyrid.}$), 7.64 d (1H, γ-$CH_{pyrid.}$, $^3J_{HH}$ 7.2 Hz), 8.46 d (1H, α-$CH_{pyrid.}$, $^3J_{HH}$ 4.4, 7.2 Hz), 8.54 s (1H, α-$CH_{pyrid.}$). ^{13}C NMR spectrum, δ_C, ppm ($CDCl_3$): 19.38 (γ-$CH_{2pypreid.}$), 25.12 d (CH_2P, $^1J_{CP}$ 135.3 Hz), 25.62 (β-$CH_{2pyperid.}$), 27.59 (β-$CH_{2pyperid.}$), 42.71 (α-$CH_{2pyperid.}$), 51.97 (α-$CH_{pyperid.}$), 52.76 d (CH_3O, $^2J_{CP}$ 7.9 Hz), 123.32 (=NC$CH_{arom.}$), 123.42 (β-$CH_{pyrid.}$), 127.01 (=NC), 128.70 (ClC$CH_{arom.}$), 134.95 (γ-$CH_{pyrid.}$), 135.76 (β-$C_{pyrid.}$), 147.26 (α-$CH_{pyrid.}$), 148.30 (α-$CH_{pyrid.}$), 149.01 (CCl), 150.95 d (C=N, $^2J_{CP}$ 7.1 Hz). ^{31}P NMR spectrum, δ_P, ppm ($CDCl_3$): +23.27.

Anabasyl-*N*-(4-methoxyphenyl)dimethoxyphosphorylacetamidine (IIb) was prepared similarly from 1.23 g (0.0042 mol) of dimethyl anabasylethynephosphonate and 0.52 g (0.0042 mol) *p*-anisidine. ^1H NMR spectrum, δ_H, ppm ($CDCl_3$): 1.60–1.68 m (6H, β,β,γ-$CH_{2pyperid.}$), 3.16 d (1H, CH_2P, $^2J_{HP}$ 22.2 Hz), 3.20 d (1H, CH_2P, $^2J_{HP}$ 22.2 Hz), 3.58 d (3H, CH_3OP, $^3J_{HP}$ 11.0 Hz), 3.64 d (3H, CH_3OP, $^3J_{HP}$ 11.0 Hz), 3.72 s (3H, CH_3O), 3.73 d (1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 10.8 Hz), 3.79 d (1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 10.8 Hz), 5.93 m (1H, α-$CH_{pyperid.}$), 6.63 d (2H, =NC$CH_{arom.}$, $^3J_{HH}$ 8.4 Hz), 6.77 d (2H, $CH_3OCCH_{arom.}$, $^3J_{HH}$ 8.4 Hz), 7.25 m (1H, β-$CH_{pyrid.}$, $^3J_{HH}$ 4.2, 7.6 Hz), 7.63 d (1H, γ-$CH_{pyrid.}$, $^3J_{HH}$ 7.6 Hz), 8.44 d (1H, α-$CH_{pyrid.}$, $^3J_{HH}$ 4.2 Hz), 8.54 s (1H, α-$CH_{pyrid.}$). ^{13}C NMR spectrum, δ_C, ppm ($CDCl_3$): 19.50 (γ-$CH_{2pyperid.}$), 24.94 d (CH_2P, $^1J_{CP}$ 135.4 Hz), 25.69 (β-$CH_{2pyperid.}$), 27.73 (β-$CH_{2pyperid.}$), 42.63 (α-$CH_{2pyperid.}$), 51.94 (α-$CH_{pyperid.}$), 52.87 d (CH_3OP, $^2J_{CP}$ 6.6 Hz), 55.35 (CH_3O), 114.18 (=NC$CH_{arom.}$), 122.61 ($CH_3OCCH_{arom.}$), 123.26 (β-$CH_{pyrid.}$), 134.76 (γ-$CH_{pyrid.}$), 135.99 (β-$C_{pyrid.}$), 143.87 (=$NC_{arom.}$), 147.26 (α-$CH_{pyrid.}$), 148.67 (α-$CH_{pyrid.}$), 151.00 d (C=N, $^2J_{CP}$ 6.8 Hz), 154.44 ($CH_3OC_{arom.}$). ^{31}P NMR spectrum, δ_P, ppm ($CDCl_3$): +22.88.

Anabasyl-*N*-(4-acetophenyl)dimethoxyphosphorylacetamidine (IIc) was prepared similarly from 1.23 g (0.0042 mol) of dimethyl anabasylethynephosphonate and 0.56 g (0.0042 mol) of *p*-aminoacetophenone. ^1H NMR spectrum, δ_H, ppm ($CDCl_3$): 1.45–1.64 m (6H, β,β,γ-$CH_{2pyperid.}$), 2.48 s (3H, CH_3CO), 3.08 d (1H, CH_2P, $^2J_{HP}$ 22.2 Hz), 3.12 d (1H, CH_2P, $^2J_{HP}$ 22.2 Hz), 3.61 d (3H, CH_3OP, $^3J_{HP}$ 11.8 Hz), 3.56 d (3H, CH_3OP, $^3J_{HP}$ 11.8 Hz), 3.70 d (1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 10.6 Hz), 3.76 d (1H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 10.6 Hz), 5.92 m (1H, α-$CH_{pyperid.}$), 6.72 d (2H, =NC$CH_{arom.}$, $^3J_{HH}$ 9.0 Hz), 6.77 d (2H, $CH_3OCCH_{arom.}$, $^3J_{HH}$ 9.0 Hz), 7.43 m (1H, β-$CH_{pyrid.}$, $^3J_{HH}$ 5.0, 7.6 Hz), 7.63 d (1H, γ-$CH_{pyrid.}$, $^3J_{HH}$ 7.6 Hz), 8.44 d (1H, α-$CH_{pyrid.}$, $^3J_{HH}$ 5.0 Hz), 8.54 s (1H, α-$CH_{pyrid.}$). ^{13}C NMR spectrum, δ_C, ppm ($CDCl_3$): 19.29 (γ-$CH_{2pyperid.}$), 25.42 d (CH_2P, $^1J_{CP}$ 135.1 Hz), 25.60 (β-$CH_{2pyperid.}$), 26.17 (CH_3), 27.58 (β-$CH_{2pyperid.}$), 42.70 (α-$CH_{2pyperid.}$), 52.01 (α-$CH_{pyperid.}$), 52.82 d (CH_3O, $^2J_{CP}$ 6.6 Hz), 121.80 (=NC$CH_{arom.}$), 123.30 (β-

$CH_{pyrid.}$), 129.52 ($CH_3C(O)C_{arom.}$), 131.04 ($CH_3C(O)CCH_{arom.}$), 134.63 (γ-$CH_{pyrid.}$), 135.39 (β-$C_{pyrid.}$), 147.59 (α-$CH_{pyrid.}$), 148.52 (α-$CH_{pyrid.}$), 149.98 d (C=N, $^2J_{CP}$ 6.7 Hz), 155.40 (=$NC_{arom.}$), 196.92 (C=O). ^{31}P NMR spectrum, δ_P, ppm ($CDCl_3$): +23.02.

Dimethoxyphosphorylacetoanabaside (III). To a solution of 0.005 mol of anabasylethynephosphonate in anhydrous carbon tetrachloride was added 0.0055 mol of distilled water. The reaction mixture was stirred vigorously for 0.5–1 h at room temperature. The solvent was evaporated in the water-jet pump vacuum. The residue is a colored viscous liquid. Yield 1.36 g (87%). ^{1}H NMR spectrum, δ_H, ppm (DMSO): 1.26–1.71 m (6H, β,β,γ-$CH_{2pyperid.}$), 3.23 d (1H, CH_2P, $^2J_{HP}$ 21.4 Hz), 3.26 d (1H, CH_2P, $^2J_{HP}$ 21.4 Hz), 3.66 d (3H, CH_3O, $^3J_{HP}$ 11.2 Hz), 3.68 d (3H, CH_3O, $^3J_{HP}$ 11.2 Hz), 3.86 d (2H, α-$CH_{2pyperid.}$, $^3J_{HH}$ 10.8 Hz), 5.76 m (1H, α-$CH_{pyperid.}$), 7.36 m (1H, β-$CH_{pyrid.}$, $^3J_{HH}$ 4.8, 7.2 Hz), 7.62 d (1H, γ-$CH_{pyrid.}$, $^3J_{HH}$ 7.2 Hz), 8.45 d (1H, α-$CH_{pyrid.}$, $^3J_{HH}$ 4.8 Hz), 8.52 s (1H, α-$CH_{pyrid.}$). ^{13}C NMR spectrum, δ_C, ppm (DMSO): 18.86 (γ-$CH_{2pyperid.}$), 25.26 (β-$CH_{2pyperid.}$), 27.14 (β-$CH_{2pyperid.}$), 31.56 d (CH_2P, $^1J_{CP}$ 130.9 Hz), 42.20 (α-$CH_{2pyperid.}$), 49.09 (α-$CH_{pyperid.}$), 52.70 d (CH_3O, $^2J_{CP}$ 6.8 Hz), 123.60 (β-$CH_{pyrid.}$), 134.51 (γ-$CH_{pyrid.}$), 140.65 (β-$C_{pyrid.}$), 147.62 (α-$CH_{pyrid.}$), 148.07 (α-$CH_{pyrid.}$), 164.28 d (C=O, $^3J_{CP}$ 3.8 Hz). ^{31}P NMR spectrum, δ_P, ppm (DMSO): +24.53.

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