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LETTERS TO THE EDITOR

To the 80th Anniversary of B.I. Ionin

Dihydrofuropyridines in Reactions of Pyridoxal Imine with 2-Chloro-1,3,2-dioxaphosphorinanes

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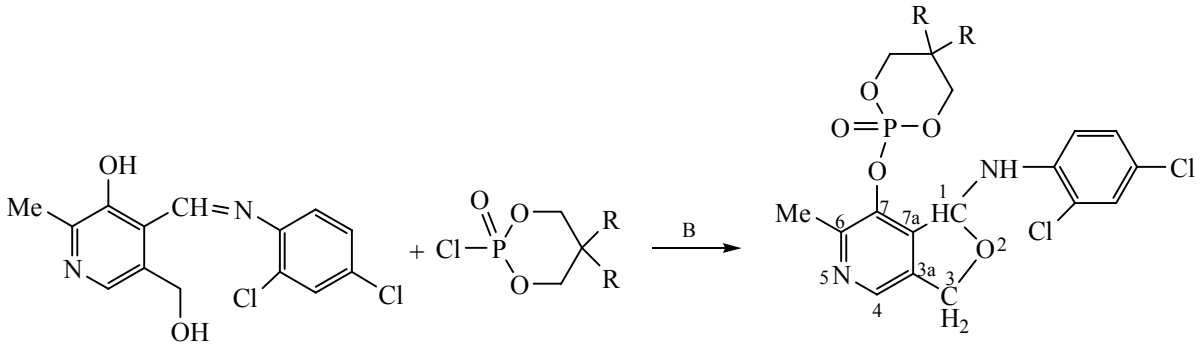
Pyridoxal (vitamin B_6) molecule contains several functional groups opening wide opportunities for its modification. For instance, synthesis of a series of substituted derivatives exhibiting biological activity has been described in [1–3].

In the present work, we used azomethine derivatives of pyridoxal as core compounds [4, 5]. Due to the presence of phenolic, hydroxyl, and imine groups, compound **I** could be transformed into the linear or cyclic products in the course of phosphorylation. 2-Chloro-2-oxo-1,3,2-dioxaphosphorinane **IIa** and 2-chloro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane **IIb** were used as phosphorylating agents. The reaction of imine **I** with acid chloride **IIa** was performed in acetonitrile (solvent) in the presence of potassium carbonate (base). In the case of di-1,3,2-oxaphosphorinane **IIb,** benzene and triethylamine were used as a solvent and a base, respectively (Scheme 1).

The reaction gave polycyclic derivatives **IIIa** and **IIIb** with yield of 76 and 58%, respectively. The composition and structure of compounds **IIIa** and **IIIb** were confirmed by elemental analysis, IR, NMR spectroscopy, and mass spectrometry data. No absorption bands of azomethine fragment were observed in IR

Scheme 1.



R= H (**a**), Me (**b**).

spectra of **IIIa** and **IIIb**. Chemical shifts of phosphorus in the ^{31}P NMR spectra were in the range of 11–14 ppm.

1-(2,4-Dichlorophenylamino)-6-methyl-7-{(2-oxodihydro-1,3-dioxaphosphorin-2-yl)oxy]-1,3-dihydrofuro[3,4-*c*]pyridine (IIIa). A mixture of 0.31 g of imine **I**, 0.15 g of anhydrous potassium carbonate, 0.16 g chlorophosphite **IIa**, and 15 mL of acetonitrile refluxed during 3 h. After cooling, the formed precipitate was filtered off, and the solvent was evaporated. 20 mL of hexane was added to the residue, and the resulting mixture was heated during 1 h. The formed precipitate was filtered off and recrystallized from acetone. Yield 0.33 g (76%), mp 111–112°C. IR spectrum, ν, cm^{-1}: 1310 (P=O), 3220–3470 (NH). ^1H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 2.53 s (3H, CH_3), 2.63 m (2H, CH_2), 4.03 m (4H, CH_2O), 4.58 d ($1H^a$, CH_2O, $^2J_{HH}$ 12.47), 4.68 d ($1H^б$, CH_2O, $^2J_{HH}$ 12.47), 5.26 s (1H, CH), 6.48 m and 7.15 m (2H, CH_{Ar}), 7.81 s (1H, CH_{Ar}), 8.37 s (1H, C^4H). ^{31}P NMR spectrum (acetone-d_6): δ_P 11.39 ppm. Mass spectrum (MALDI-TOF): *m*/*z* 430 [*M* – 1]. Found, %: C 47.19; H 3.86; N 6.62; P 7.14. $C_{17}H_{17}Cl_2N_2O_5P$. Calculated, %: C 47.33; H 3.94; N 6.50; P 7.19.

1-(2,4-Dichlorophenylamine)-6-methyl-7-{(2-oxo-5,5-dimethyldihydro-1,3-dioxaphosphorin-2-yl)oxy]-1,3-dihydrofuro[3,4-*c*]pyridine (IIIb). A mixture of 0.62 g of imine **I**, 0.21 g of triethylamine, 0.37 g of chlorophosphite **IIb**, and 10 mL of benzene was refluxed during 2 h. Triethylamine hydrochloride was separated off, the solvent was evaporated, and the residue was dissolved in 12 mL of benzene–hexane mixture (1 : 1). The resulting mixture was heated during 6 h, and then the precipitate was filtered off. Yield 0.53 g (58%), mp 115–117°C. IR spectrum, ν, cm^{-1}: 1291 (P=O), 3205–3480 (NH). ^1H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 0.85 s (3H CH_3), 1.23 s (3H CH_3), 2.58 s (3H CH_3), 4.03 m (4H, CH_2O), 4.57 d ($1H^a$, CH_2O, $^2J_{HH}$ 12.44), 4.66 d ($1H^b$, CH_2O, $^2J_{HH}$ 12.44), 5.25 s (1H, CHO), 6.46, 7.12 (2H, CH_{Ar}), 7.84 s (1H, CH_{Ar}), 8.33 s (1H, C^4H). ^{31}P NMR spectrum (acetone-d_6): δ_P 13.85 ppm. Mass spectrum (MALDI-TOF): *m*/*z* 460 [*M* + 1]. Found, %: C 49.49; H 4.86; N 6.12; P 6.54. $C_{19}H_{21}Cl_2N_2O_5P$. Calculated, %: C 49.67; H 4.57; N 6.10; P 6.75.

IR spectra were recorded with a Bruker Vector-22 spectrometer (400–3600 cm^{-1}, KBr pellets). ^1H NMR spectra were registered with an Avance 600 instrument operating at of 600.13 MHz referenced to the residual proton signals of the deuterated solvent. ^{31}P NMR spectra were obtained using a Bruker MSL-400 spectrometer (100.62 MHz). Mass spectra (MALDI-TOF) were recorded with an Ultraflex III TOF/TOF Bruker instrument (*p*-nitroaniline as matrix).

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