

SHORT
COMMUNICATIONS

Synthesis of Phospholipids on the Basis of 2-Hydroxymethyl-2-propyl-1,3-propanediol

G. A. Savin¹, E. A. Kamneva¹, and E. E. Nifant'ev²

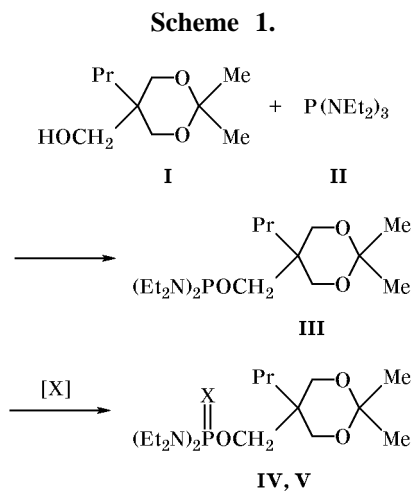
¹ Volgograd State Pedagogical University, pr. Lenina 27, Volgograd, 400131 Russia

² Moscow State Pedagogical University, Moscow, Russia

Received January 10, 2003

Analogues of naturally occurring phospholipids are readily accessible substrates which are suitable for various biophysical studies [1]. Among these compounds, an important group includes lipids modified at the alcohol fragment.

We have synthesized first representatives of previously unknown phosphatide acids on the basis of 2-hydroxymethyl-2-propyl-1,3-propanediol. Initially, two hydroxy groups in 2-hydroxymethyl-2-propyl-1,3-propanediol were protected by treatment with acetone, and compound **I** was phosphorylated with hexaethylphosphorous triamide (**II**) to obtain phosphorodi-amidite **III** (Scheme 1).



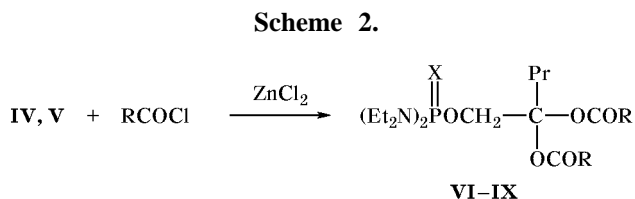
The reaction was carried out at 90–100°C over a period of 2 h with simultaneous removal of the released diethylamine by distillation under reduced pressure (380 mm). The progress of the reaction was monitored by TLC and ³¹P NMR spectroscopy. The

resulting 2,2-dimethyl-5-propyl-5-(tetraethyldiamino-phosphinoxymethyl)-1,3-dioxane (**III**), δ_P 134 ppm, R_f 0.4 [benzene–dioxane, 10:1 (A), Silufol UV-254], was converted (without purification) into the corresponding thio and seleno derivatives **IV** and **V** by treatment with sulfur or selenium. Compounds **IV** and **V** were purified by column chromatography on silica gel using benzene as eluent.

2,2-Dimethyl-5-propyl-5-(tetraethyldiamino-phosphinothioyloxymethyl)-1,3-dioxane (IV). Yield 64%, $n_D^{20} = 1.4850$; δ_P 79 ppm; R_f 0.65 (A).

2,2-Dimethyl-5-propyl-5-(tetraethyldiamino-phosphinoselenoyloxymethyl)-1,3-dioxane (V). Yield 72%; $n_D^{20} = 1.5008$; δ_P 81 ppm ($^1J_{P,Se} = 840$ Hz); R_f 0.65 (A).

Compounds **IV** and **V** were then acylated with myristoyl and stearoyl chlorides at 20°C in the presence of a catalytic amount of anhydrous zinc(II) chloride according to the procedure described in [2] (Scheme 2).



VI, R = C₁₃H₂₇, X = S; **VII**, R = C₁₃H₂₇, X = Se; **VIII**, R = C₁₇H₃₅, X = S; **IX**, R = C₁₇H₃₅, X = Se.

Diesters **VI–IX** were isolated in up to 52% yield by column chromatography on silica gel using hexane as eluent.

1,3-Dimyristoyloxy-2-propyl-2-(tetraethyldiamino-phosphinothioyloxymethyl)propane (VI). Oily substance, R_f 0.55 (A).

1,3-Dimyristoyloxy-2-propyl-2-(tetraethyl-diaminophosphinoselenoyloxymethyl)propane (VII). Oily substance, R_f 0.55 (A).

1,3-Distearoyloxy-2-propyl-2-(tetraethyl-diaminophosphinothioyloxymethyl)propane (VIII). mp 48–49°C, R_f 0.55 (A).

1,3-Distearoyloxy-2-propyl-2-(tetraethyl-diaminophosphinoselenoyloxymethyl)propane (IX). mp 29–30°C, R_f 0.55 (A).

The ^{31}P NMR spectra of diacyl derivatives **VI–IX** were similar to those of the corresponding initial compounds **IV** and **V**. Their structure and purity were confirmed by elemental analyses, ^1H and ^{31}P NMR spectra, and TLC. The ^1H NMR spectra of 0.5 M

solutions of compounds **I** and **IV–IX** in CDCl_3 were recorded on a Bruker WM-250 spectrometer at 250 MHz. The ^{31}P NMR spectra of compounds **III–IX** in benzene were measured on a Bruker WP-80SY instrument (32.4 MHz) relative to 85% H_3PO_4 as external reference.

REFERENCES

1. Evstigneeva, R.P., Zvonkova, E.N., Serebrennikova, G.A., and Shvets, V.I., *Khimiya lipidov* (Chemistry of Lipids), Moscow: Khimiya, 1983.
2. Nifant'ev, E.E. and Predvoditelev, D.A., *Usp. Khim.*, 1997, vol. 66, p. 47.