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SHORT COMMUNICATIONS

Substituted 4,5-Dihydrooxazoles in the Synthesis of New Phospholipids

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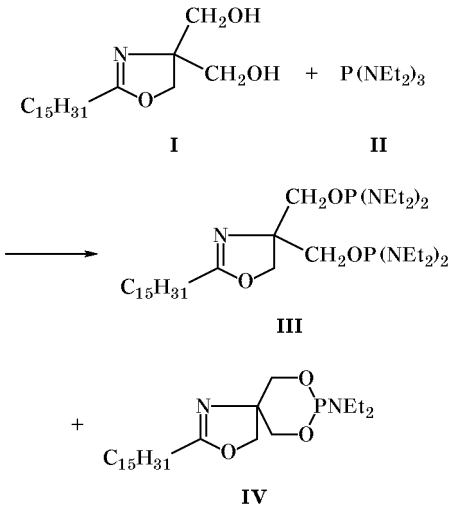
In continuation of our studies on the synthesis of new lipid structures on the basis of amino alcohols [1], we now report on the preparation of previously unknown substituted dihydrooxazole-containing phosphates which are the first reperesentatives of a new class of phospholipids. As starting compounds we used a readily accessible derivative of tris(hydroxymethyl)aminomethane, 4,4-bis(hydroxymethyl)-2-pentadecyl-4,5-dihydrooxazole (**I**).

In the first step of the study, heterocyclic diol **I** [mp 103–104°C; R_f 0.5 (Silufol UV-254, chloroform–methanol, 10:1, system A)] was phosphorylated with hexaethylphosphorous triamide (**II**) to obtain a mixture of bis-phosphorodiamidite **III** and phosphoroamidite **IV** (Scheme 1).

Scheme 1.



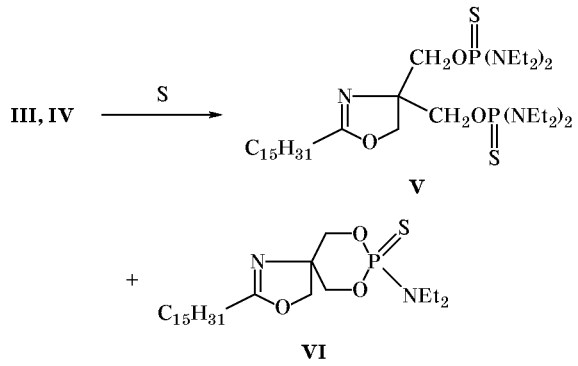
The progress of the reaction was monitored by TLC and ^{31}P NMR spectroscopy.

4,4-Bis(*N*,*N*,*N*′,*N*′-tetraethyldiaminophosphinoxymethyl)-2-pentadecyl-4,5-dihydrooxazole (III). R_f 0.8 (benzene–dioxane, 5:1, system B); δ_P 134 ppm.

2′-Diethylamino-2-pentadecyl-4,5-dihydrooxazole-4-spiro-5′-1,3,2-dioxaphosphinane (IV). R_f 0.72 (B); δ_P 146 ppm.

Compounds **III** and **IV**, without isolation from the reaction mixture, were converted into the corresponding phosphoramidothioates **V** and **VI** by the action of elemental sulfur (Scheme 2).

Scheme 2.



Products **V** and **VI** are characterized by different chromatographic mobilities, and they were separated by column chromatography on silica gel using benzene as eluent. The yield of **V** and **VI** depends on the molar ratio of dihydrooxazole **I** and phosphorylating agent **II**. When the **I**-to-**II** molar ratio was 1:1, the yield of **V** and **VI** was 8 and 49%, respectively. In the presence of 2 equiv of phosphorous triamide **II**, the yield of **V** reaches 43%, and that of **VI**, 15% (on the initial diol **I**).

4,4-Bis(*N*,*N*,*N*′,*N*′-tetraethyldiaminophosphinothioyloxymethyl)-2-pentadecyl-4,5-dihydrooxazole

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(V). mp 32–33°C; δ_P 79 ppm; R_f 0.45 (hexane–dioxane, 10 : 1, system C).

2′-Diethylamino-2-pentadecyl-4,5-dihydrooxazole-4-spiro-5′-1,3,2λ^5-dioxaphosphinane 2′-sulfide (VI). mp 53–54°C; δ_P 75 ppm; R_f 0.4 (C).

The structure of the products was proved by elemental analyses and ^{31}P and ^1H NMR spectra, and their purity was checked by TLC.

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REFERENCE

1. Predvoditelev, D.A., Savin, G.A., and Nifant'ev, E.E., *Russ. J. Org. Chem.*, 1995, vol. 31, p. 461.