

Synthesis of 1,3,2-Dioxoazaphospholanes

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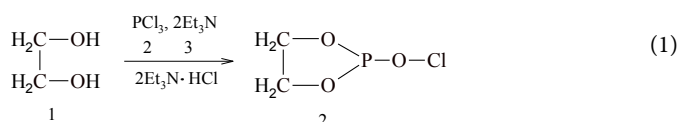
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Introduction

The chemistry of phospholanes gained broad development first of all due to their many useful properties as the intermediate readily available monomeric substances with functional groups and various heteroatoms and also having particular biological properties [1,2]. Phospholane cycle is a part of the biologically active synthetic material. In addition, it is a structural basis of many antimicrobial tools, thus researchers are interested in these systems [3-5].

With the purpose of obtaining new 1,3,2-dioxoazaphospholanes, the following compounds are used as starting reagents: ethylene glycol, phosphorus trichloride, alcohols, monoethanol amine vinyl ether. These substances are readily available monomers of chemical production. They are not waste products, but are monomers for obtaining different chemicals. The novelty of this work is that in order to obtain new phospholanes for the first time we used vinyl monoethanol amine ether. For the first time we obtained 1,3,2-dioxoazaphospholanes.

The aim of this work was to develop preparative aspects of the formation reactions of phospholane series compounds at interaction of chlorine-containing phospholanes with monoethanolamine vinyl ether, which would extend preparative capabilities using a known method and obtain previously unknown 1,3,2-dioxoazaphospholanes. Chlorides of ethyleneglycolphosphorus acid were taken as initial reagents. They were obtained by phosphorylation of ethylene glycol by means of phosphorus trichloride according to the scheme:



In the series of phosphorous organic compounds, 1,3,2-dioxoazaphospholanes have a huge potential as a synthetic materials, and are interesting objects to study different types of biological activities.

In the course of the experiment, we have successively obtained the compounds indicated in the article.

Experimental Section

O,O-Dipropyl - {N-2-(vinylloxy), ethylamido}thiophosphate

4.55 g (0.025 mol) of thiophosphite O,O-dipropyl was added to benzene solution of 2.17 g (0.025 mol) of monoethanolamine vinyl ether, 2.5 g (0.025 mol) of triethylamine and 3.84 g (0.025 mol) of CCl₄ under stirring and a temperature of 18°C. Hydrochloride of triethylamine precipitated in process of cooling of a reaction mixture. The sediment was filtered, then the filtrate was boiled out in vacuo, the rest was investigated on a chromatograph with a column with a silica gel, eluent-hexane-acetone (3:1).

O,O-diisopropyl-, O,O-dibutyl-, O-isopropyl (piperidyl) [N-2-vinylloxyethylamido]thiophosphate and O-butyl (piperidyl) [N-2-vinylloxyethylamido]thiophosphate were received similarly.

The purity of the compounds and the reactions were monitored by TLC on Silufol UV 254 plates in specified eluents systems. The manifestation was carried out with iodine vapor.

³¹P NMR spectra was recorded on the “Bruker WP-200SY” device with an operating frequency on nuclei ³¹P 81.01 MHz; external standard - 85% solution of H₃PO₄.

Synthesis of 2-chloro-1,3,2-dioxaphospholane

50 ml of anhydrous ether, 9.3 g of ethylene glycol and 22.0 g of pyridine were placed in the reaction flask. 20.62 g of phosphorus trichloride was added to the reaction mixture with stirring at a temperature of -16 to -17°C. After the addition of phosphorus trichloride at room temperature, the solution was left with stirring for about 1.5 h. During the reaction, the pyridine hydrochloride formed. The ether solution of 2-chloro-1,3,2-dioxaphospholane was isolated by filtration. Further desired product 2-chloro-1,3,2-dioxaphospholane was obtained by simple distillation. Boiling point=56°C, 1.4917; Molecular Weight=126.49; Gross formula: C₂H₄PO₂Cl.

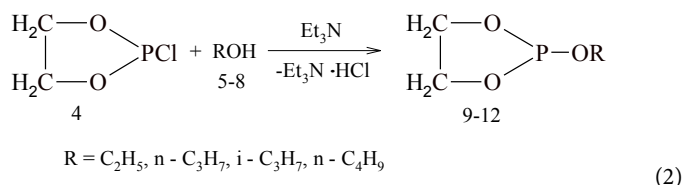
- Synthesis of 2-alkoxy-1,3,2-dioxaphospholanes
- Synthesis of 2-ethoxy-1,3,2-dioxaphospholanes

30 l of absolute diethyl ether, 1.72 g of ethanol, 2.96 g of pyridine were placed in a reaction flask.

Results and Discussion

The foundation of researches in the field of 1,3,2-dioxaphospholane is laid in Arbuzov and Kabachnik's works [6,7].

We investigated reactions of alkyl-1,3,2-dioxaphospholanes with monoethanolamine vinyl ethers, which, in the result, leads to formation of series of 1,3,2-dioxaphospholanes vinyl ethers derivatives. Firstly we synthesized the phosphorous acid ethyleneglycol chloride [8] and further corresponding alkyl-1,3,2-dioxaphospholanes were obtained on its basis according to the following scheme:



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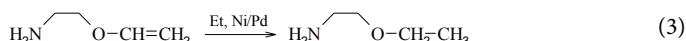
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In order to obtain polyfunctional derivatives of phosphorous acid diols, in our investigations we used the chemical monomer of series of amino alcohols vinyl ethers-monoethanolamine vinyl ether. Due to the presence of amino- and vinyloxy groups these compounds have a great synthetic potential of amines and vinyl ethers. Vinyl ethers and their derivatives are of great interest as monomers for synthesis of polyfunctional compounds, which are widely used as chemotherapeutic drugs, polymer materials, pesticides, plant growth stimulators.

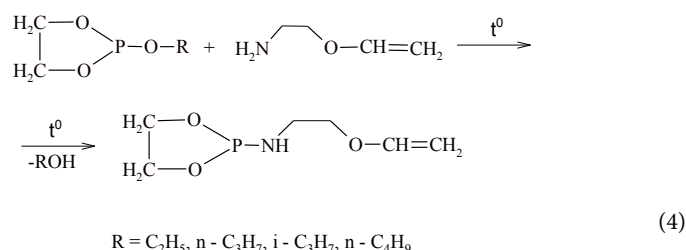
In the industry, ethoxyethylamine were obtained by catalytic hydrogenation on the basis of monoethanolamine vinyl ether. Ethoxyethylamine were used in synthesis of anti-diabetic medicines. The scheme of this medicinal preparation is given below:



The synthesized vinyl ethers of Schiff's bases are of interest as polyfunctional monomer compounds for the development of the theory and practice of functionally substituted vinyl ethers of amino alcohols, and for the further development of targeted methods of new biologically active derivatives synthesis on their basis having a set of properties that are important for practical applications. The researches of properties of a number of Schiff's bases containing amino groups, various on character [8-14] were conducted in order to clarify the relationship between the structure and reactivity of vinyl ethers of amino alcohols. Studying the properties and synthetic opportunities of amino alcohols vinyl ethers and their derivatives, the research on properties of a monoethanolamine vinyl ether monomer in reaction with phosphoric-acid-diols were continued.

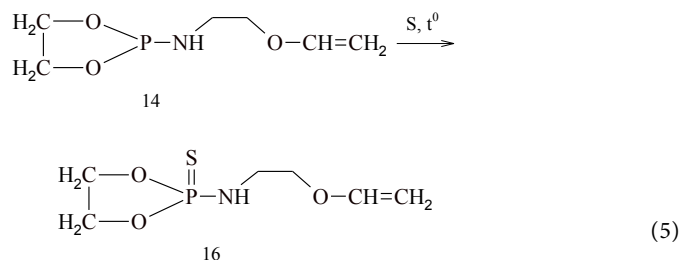
Earlier we studied condensations of monoethanolamine vinyl ether with various carbonyl compounds, the corresponding Schiff's bases were received [15-23].

With a view to expand the series of polyfunctional and heteroatom-containing derivatives of amino alcohols vinyl ethers, including monoethanolamine vinyl ether, the series of derivatives of 1,3,2-dioxaphospholanes vinyl ethers was synthesized in the result of interaction between alkyl-substituted diols of phosphorous acid with monoethanolamine vinyl ether:

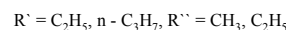
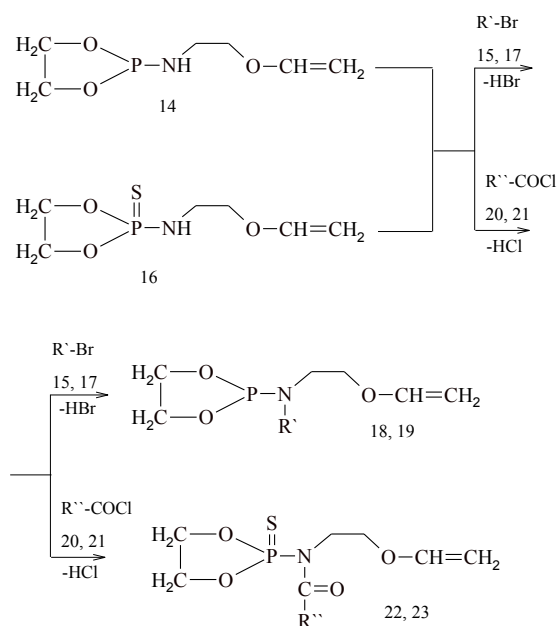


Molecules of 1,3,2-dioxaphospholane vinyl ethers derivatives contain reactive secondary amino groups and vinyloxy group. The presence of trivalent phosphorus of dioxaphospholane cycle and the double bond in vinyloxy group cause high reactivity. Thus, organic phosphorus compounds containing R-C-N, P-O-C fragments deserve attention as effective bioactive agents, flotation agents and complexing agents. These compounds possess unique reactivity due to the mutual influence of geminal nitrogen and phosphorus atoms.

Due to our research interests in the field of organophosphorus compounds chemistry [8-10], we conducted the reaction of N-vinyloxiethyl-1,3,2-dioxaphospholane with elemental sulfur, which resulted in the corresponding synthesized thiophospholane:

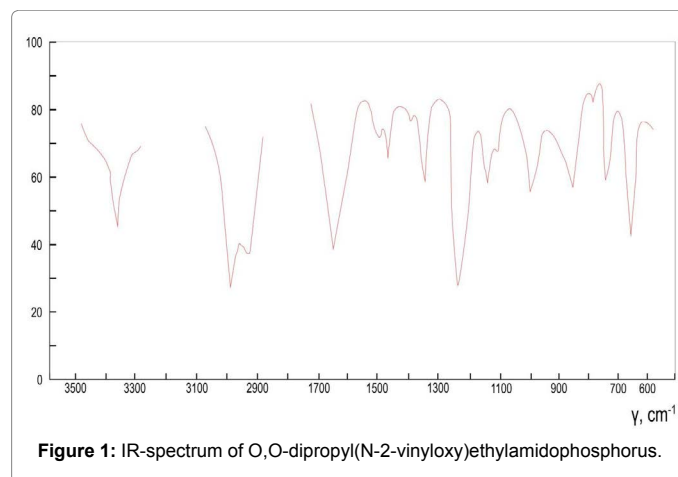


Reactions of alkylation and acylation were carried out in order to elucidate the reactivity of synthesized 1,3,2-dioxathio-phospholanes. As a result, the corresponding alkyl and acyl derivatives of phospholanes were obtained:



The structure of the obtained substances was confirmed by ³¹P-NMR and IR spectroscopy. IR spectra (δ): P=S (630-650), P-N (890-920), P-O-C (1135-1180), C=C (1605-1625), N-H (3260-3280) (Figures 1-3).

³¹P NMR spectra -(1H) [m.d.]:Pr n 72.40 (c), Pr iso 72.84(c), Bu n 72.90(c), Pr iso PP piperidyl- 74.10(c), Bu n PP piperidyl 73.90(c).



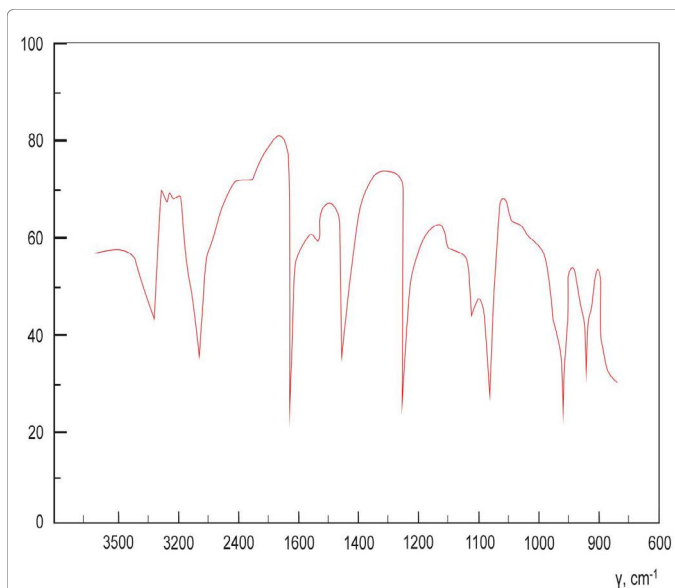


Figure 2: IR-spectrum of o-butyl(piperidyl)-N-2-(vinylxyethylamido)-thiophosphorus.

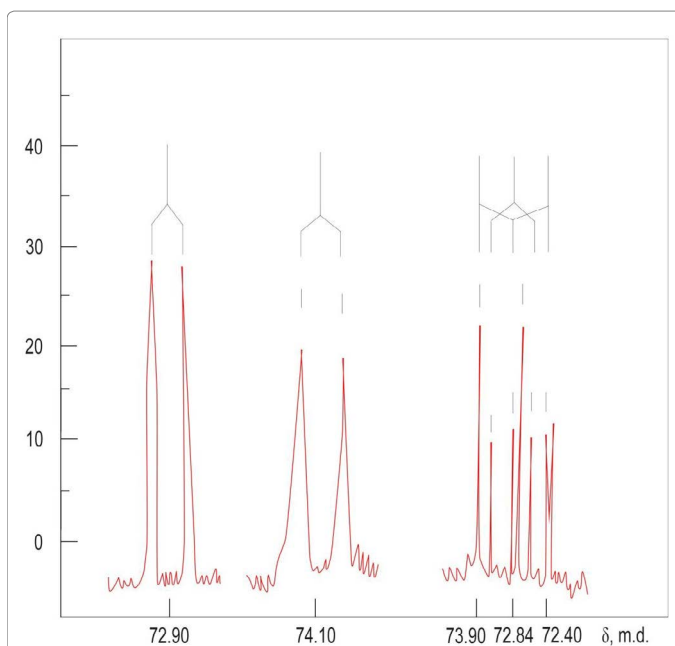


Figure 3: NMR 31P spectrum of O-i-propyl-[N-2-vinylxyethylamid] thiophosphorus.

IR spectra were obtained on a spectrophotometer UR-20. 31P NMR spectra were recorded on the instrument "Bruker WP-200 SY" (81.01 MHz, the standard- 85% H₃PO₄)

Currently, the biological activity of the compounds is studied by computer prediction; structure is studied by the quantum chemistry method

Conclusion

In the process of phosphorylation of ethylene glycol in the presence of phosphorus trichloride and alcohols, cyclic alkyl derivatives of phospholanes were synthesized. On the basis of cyclic phospholanes and vinyl ether monoethanol amine, amine derivatives of phospholanes were first obtained. Subsequently, cyclic amino derivatives of phospholanes

undergo an acylation reaction. In the result, acyl derivatives of cyclic phospholanes and their thio derivatives were synthesized.

The importance from the theoretical point of view of the amino derivatives of cyclic phospholanes are promising chemical monomers. Since the molecule contains vinyloxy and a secondary amine group. 1,3,2-dioxazaphospholanes form a class of biologically active substances and can have antibacterial properties.

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