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LETTERS TO THE EDITOR

Dedicated to the 115th anniversary of B.A. Arbuzov's birth

1-(3,3-Diethoxypropyl)-1-[(dihexylphosphoryl)methyl]-3-phenylurea in the Synthesis of 4-Aryl-Substituted Tetrahydropyrimidin-2-ones

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Abstract—First specimens of 4-aryl-substituted tetrahydropyrimidin-2(1*H*)-ones containing a phosphoryl group were obtained through the reaction of 1-(3,3-diethoxypropyl)-1-[(dihexylphosphoryl)methyl]-3-phenylurea with resorcinol and its derivatives in the presence of trifluoroacetic acid.

Keywords: aminophosphine oxides, ureidoacetals, condensation, resorcinol

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Development of methods for the synthesis of functionalized pyrimidin-2-one derivatives is of considerable interest for medical chemistry. Among the representatives of these heterocycles, selective α_{1a}-adrenergic receptor antagonists, Eg5 kinesin inhibitors [1], compounds exhibiting antihypertensive [2], anti-inflammatory [3], and antiproliferative activity [4] were found. Introduction of the phosphoryl group to the structure of pyrimidin-2-ones can lead to increased pharmacological activity of these derivatives. To date, the method for producing phosphorylated dihydropyrimidines through the three-component condensation of aldehydes, urea, and *O*,*O*-dialkyl 2-oxopropanephosphonate in the presence of ytterbium triflate has been reported [5].

At the same time, β-ureidoacetals are promising synthons for the construction of six-membered heterocycles. The only example of the condensation of β-ureidoacetal with 2,6-dimethylphenol in an acidic medium resulting in tetrahydropyrimidin-2-one with anti-inflammatory activity has been known[6].

Recently, we have developed methods for the synthesis of phosphorylated aminoacetals, synthons for the synthesis of phosphorylated aryl-substituted heterocycles [7, 8]. Here we report for the first time the synthesis of new phosphorus-containing tetrahydropyrimidin-2-ones. Thus, the reaction of phosphorylated aminoacetal **1** with phenyl isocyanate afforded β-ureidoacetal **2** containing a phosphine oxide group (Scheme 1). The acid-catalyzed condensation of **2** with resorcinol and its derivatives like pyrogallol, 2-methylresorcinol or resorcinol in the presence of 3-fold excess of trifluoroacetic acid at room temperature for 72 h furnished new phosphorylated tetrahydropyrimidin-2-ones **4a**–**4c** (Scheme 2).

The structure of the obtained compounds was proved by ^{1}H and ^{31}P NMR, IR spectroscopy; the composition was confirmed by mass spectrometry and elemental analysis.

Compound **1** was obtained by the previously described method [8].

1-(3,3-Diethoxypropyl)-1-[(dihexylphosphoryl)-methyl]-3-phenylurea (2). Phenyl isocyanate (0.50 g) was added dropwise to a solution of 1.57 g of phosphine oxide **2** in 10 mL of benzene. The reaction