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SYNTHESIS OF PHOSPHONIC ACIDS OF POLYFUNCTIONAL PYRIDOPYRIMIDINES

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Abstract. *In the article synthesized 2,3-trimethylene-3,4-dihydropyrido[2,3-d] pyrimidin-4-one from 2-Aminonicotinic acid and pyrrolidone-2 in the presence different agents, such as PCl_5, $POCl_3$. Its reduction reaction with $NaBH_4$ carrying out. Obtained 2,3-trimethylene-1,2,3,4-tetrahydropyrido[2,3-d] pyrimidin-4-one – this three-component coupling of a carbonyl, an amine and a hydrophosphoryl compoud leads to α-aminophosphonates, phosphorous acid-formaldehyde; aldehydes in three component system; minomethylphosphonic acid synthesis based on kabachnik-filds reaction. 2,3-trimethylene-3,4-dihydropyrido[2,3-d] pyrimidin-4-one 35% da product obtained. The reason of low reaction yield was studied. Structures were confirmed using IR and 1H NMR spectroscopies. Obtained product reduced using $NaBH_4$ and 2,3-trimethylene-1,2,3,4-tetrahydropyrido[2,3-d] pyrimidin-4-one synthesis was carried out with high yield. 2,3-trimethylene-1,2,3,4-tetrahydropyrido[2,3-d] pyrimidin-4-one and respective aminophosphonic acids were synthesized in three component system with high yield.*

Keywords: *2,3-trimethylene-3,4-dihydropyrido[2,3-d] pyrimidin-4-one, 2,3-trimethylene-1,2,3,4-tetrahydropyrido[2,3-d] pyrimidin-4-one, 2-Aminonicotin acid, pyrrolidone-2, Kabachnik–Filds reactions & IR spectra*

INTRODUCTION

In the world synthesis of new physiologically active derivatives of pyrido[2,3-d]pyrimidin and creation on their basis of modern medicinal facilities come with the use of high-tech. It is known that the anti-cancer drugs applied to date, destroying malignant cancer cells, simultaneously damage healthy cells.

Representatives of pyrido[2,3-d]pyrimidins is preferentially operating anti-cancer drugs of palbocyclik, preparations of antibacterial action of pipemidic and piromid acids are worked out by the world scientists. These medical facilities promote practical interest in derivatives.

Organophosphous compounds are ubiquitous in nature and find applications in the fields of agriculture, medicine, and industry [1-3]. Some organophosphorus compounds are important pesticides [4], bactericides [5-7], and antibiotics [5]. Phosphorus analogues of α-pyrones act as HIV protease inhibitor [8]. α-aminophosphonic acids constitute important motifs among the organophosphorus compounds in medicinal chemistry due to their obvious structural similarities to α-amino acids [9,10]. Many natural and synthetic aminophosphonic acids and their ester and peptide derivatives display a wide range of biological activities [11,12], act as herbicides [13], enzyme inhibitors [14], and antibacterial [15,16] antiviral [10], and antitumor [17] agents, and may even be peptide mimics [18].

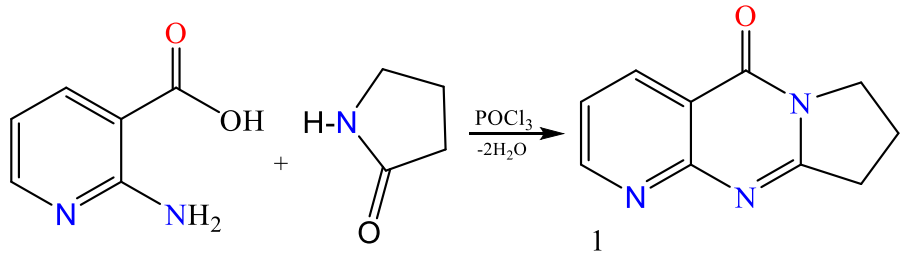
The most common synthetic route to α-aminophosphonic acids is via chemical manipulation of the corresponding α-aminophosphonates [19-21]. The hydrophosphonylation of imines is a widely used method for the synthesis of α-aminophosphonates [19-27]. This is achieved by one of two pathways: (I) in a two-component fashion known as the Pudovik reaction [28,29]

or (II) by the Kabachnik-Filds reaction [22, 23, 30, 31] which combines in situ formation of imine by condensation of amines with an aldehyde or ketone and an hydrophosphonylation step [32].

One-pot Kabachnik-Filds reaction can be promoted by acidic or basic catalysts, microwave irradiation, or by heating [33]. Due to the above–mentioned factors, in this paper we reported the synthesis of α-aminophosphonates with high yield using a recyclable catalyst for applications in medicine and industry.

MATERIALS AND METHODS

Threecyclic 2,3-thremetilenpyrido[2,3-d] pyrimidin-4-one (1) was synthesized coming from 2-aminonicotinic (2-amino-3-pyridin carboxylic) acid that was exposed to condensation with pyrrolidone-2 in the presence of $POCl_3$.



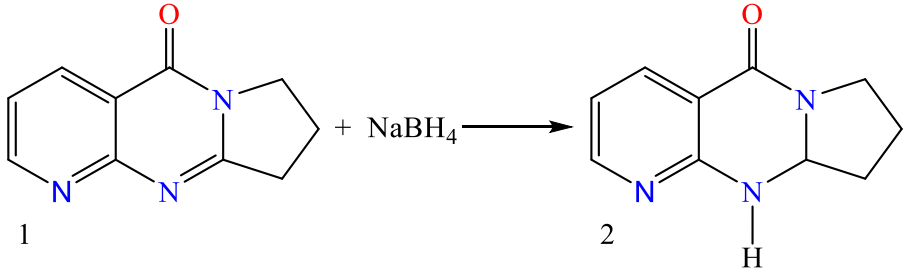
Scheme 1: Synthesis of 2,3-trimethylene-3,4-dihydro-pyrido[2,3-d]pyrimidin-4-one

Yield of products of condensation with lactam row 2-aminotiophen-3-carboxylic, 2-aminobenzoyic(antranilic) and 2-aminopyridin-3-carboxylic acids go down. So, if 2,3-threemetylentieno[2,3-d]-pyridin-4-one is got with 81% yield, and 2,3-polymetylen-hinazalon - with 56-70% yield, in the cases of 2,3-threemetylenpyrido-[2,3-d]pyrimidin-4-one (1) he made a 35%. This fact explained by that π-electron a surplus tiophenic ring facilitates, and π-deficit pyridinic ring hampers flowing of this condensation.

In infrared spectrum 1 there are absorptions bands characteristic for amido carbonyl groups (N-C=O) in area of 1683 cm^{-1}, and absorption bands of C2=N1 double bond show up in area of 1625 cm^{-1}.

In 1H NMR spectrum 1 (CDCl3) aromatic protons are observed in the weak fields at 7.31-7.34 ppm in a kind duplicate of duplicates (1H, dd, J=4.6, 7.9, H-6), 8.48-8.53 (1H, ppm J=2.0, 7.9, H-5) and 8.86-8.89 (1H, ppm, J=2.0, 4.6, H-7).

Selective reduction of N1=C2 bonds. Reduction of 2,3-three-metylenopyrido[2,3-d] by the pyrimidin-4-one (1) borhydrid of natrium in a spirit solution at boiling results in formation of 2,3-threemytilen-1,2,3,4-tetrahydropyrido[2,3-d]pyrimidin-4-on (2). In this case, selective reduction goes N1=C2 to double bonds of pyrimidinic ring, and carbonyl group C=O in position 4 remains.



Scheme 2. Reactions of 1 with $NaBH_4$

CONCLUSIONS

The new method of preparation of 2,3-threemytilenpyrido[2,3-d]-pyrimidin-4-one condensation of 2-aminonicotinic acid with lactam.

Carries out selective renewal of N1=C2 double bonds of 2,3-threemytilenpyrido[2,3-d]-pyrimidin-4-one.

The synthesis of new α-aminophosphonic acid was achieved in high yields through a one-pot three-component reaction process, a Kabachnik-Filds reaction. It involves the reactions among 2,3-trimethylene-1,2,3,4-tetrahydropyrido[2,3-d]pyrimidin-4-one, substituted aromatic aldehydes, and phosphorous acid in dry toluene at reflux temperature. Their structures were determined by elemental analysis IR, 1H-NMR, and mass spectral data.

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