Synthesis and heterocyclization of z,e isomers of some nitroso group containing organophosphorus compounds.

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Abstract

The reaction of diethyl phosphite with isonitrosoacetoacetic eter and isonitrosoacetylacetone under the conditions of the Todd-Atherton reaction leads to obtaining mixture of Z and E isomers ethyl 3-(diethoxyphosphoryloxy)-2-nitroso-but-2-enoate and 4-(diethoxyphosphoryloxy) -2-nitroso-3-penten-2-on in 60 and 70% yield, respectively. The reaction of ethyl 3- (diethoxyphosphoryloxy) -2-nitrosobut-2-enoate with urea in the presence of sodium ethylate solution, is stirred at room temperature for 2 h, then refluxed 3 h giving 2,6-dihydroxy- 4-methyl-5-nitrosopyrimidine in 80 % yield.

Keywords: Cytosine, Uracil, Thymine, Purines, Antibacterial, Antiallergic.

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Description

Many pyrimidine derivatives have high biological activity and are part of drugs used in medicine, as well as a large number of pesticides used in agriculture. Compounds of the pyrimidine and purine series play an important role in ensuring the vital activity of all living organisms. This central ring as pyrimidine is itself very important member of all the diazines with profound presence in DNA and RNA in the form of cytosine, uracil, thymine and also in purines, uric acid and barbituric acid [1]. They have gained much interest in the field of drug research to design and discovery of new physiologically and pharmacologically active compounds. Annulated pyrimidine derivatives have received great attention during the past years, because they exhibit a wide range of biological activities such as antibacterial and antifungal activity, antiasthmatics, antiallergic antihypertensive, cardiotonic, bronchodilator or antitumor activity [2].

All reagents and solvents were obtained commercially from abcr GmbH and were used without further purification [3,4]. The synthesis isonitrosoacetylacetone, isonitrosoacetoacetic eter, was carried out according to the methods described in works respectively.

The 1 H, and 31P NMR spectra were registered on a Varian Mercury-300 spectrometer operating at 300.08, and 121.75 MHz for the 1 H, 31P nuclei, respectively, at 303 K relative to internal TMS (1 H) and external 85% H3PO4 (31P) [5].

Z,E)-Ethyl 3-(diethoxyphosphoryloxy)but-2-enoate (I): To a mixture of 6.9 g (0.05 mol) of diethyl phosphite, 15.4 g (0.1 mol) of carbon tetrachloride, 9.5 g (0.05 mol) of isonitrosoacetoacetic eter, and 1.06 g (0.005 mol) of triethylbutylammonium chloride was added dropwise 16 ml of 20% aqueous sodium hydroxide solution at vigorous stirring and cooling to 0°C, so that the reaction temperature did not exceed 15°C. After stirring for 3 h at room temperature the organic layer was separated and dried with Na2SO4 [6].

2,6-dihydroxy-4-methyl-5-nitrosopyrimidine (3): To a solution of sodium ethylate prepared by 0.4 g (0.017 mol) of sodium and 50 ml of absolute ethanol was added 4.5 g (0.017 mol) of (Z,E)-ethyl 3-(diethoxyphosphoryloxy)but-2-enoate stirred at room temperature for 2 h, then refluxed 3 h[7]. From the solution, 30 ml of ethanol was distilled off, the residue was neutralized with dilute hydrochloric acid. The precipitated crystals were filtered off, washed on the filter with water. Allocated crystals 3, yield 2.12 g (80%), M.p. 320-325°C. 1 H NMR spectrum (CDCl3), δ, ppm (J, Hz): 2.32 (3H, s CH3), 12.53 and 12.90 (2H br s 2-OH and 6-OH) [8].

The phosphorylation of nucleophiles by dialkylphosphites and other neutral hydrophosphoryl compounds in the presence of carbon tetrachloride and bases at the present time are fully studied. This reaction opened and investigated by Todd and Atherton probably, consists in the deprotonation of hydrophosphorylic compound under the action of base with the following transformation of the formed anion into the chloranhydride of the corresponding acid of pentavalent phosphorus. The last is acting as a the phosphorylating reagent towords to the selected nucleophile [9].

We have used the reaction of Todd - Atherton in the synthesis of some organophosphorus compounds with the use of CH-acids as the nucleophiles. Under the Todd–Atherton reaction conditions, the keto-enol CH-acids were found to be also phosphorylated on the oxygen atom. It is in agreement with the reaction course of the corresponding ambident ions with the strong electrophiles [10].

The reaction of diethyl phosphite with isonitrosoacetoacetic eter and isonitrosoacetylacetone in the presence of carbon tetrachloride, 20% aqueous alkali, and triethylbutylammonium

chloride (TEBAC) at 0–15°C followed by stirring for 3 h without cooling gave ethyl 3-(diethoxyphosphoryloxy)-2-nitroso-but-2-enoate 1 and 4-(diethoxyphosphoryloxy)-2-nitroso-3-penten-2-one II in 60 and 70% yield, respectively. According to the 1 H NMR data, compounds 1 and 2 formed as mixtures of Z,E-isomers in the ratio of 75%:25% inthe case of compound 1 and 85%:15% in the case of compound 2.

Conclusion

A method for synthesis of 2,6-dihydroxy-4-methyl-5-nitrosopyrimidine by heterocyclization ethyl 3-(diethoxyphosphoryloxy) -2-nitroso-but-2-enoate was developed.

Further it is planned to synthesize new derivatives of nitroso containing pyrimidines from organophosphorus compounds.

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