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Synthesis of heteroaryl-substituted pyrazolo[1,5-a]pyrimidines by recyclization of pyrimidinium salts

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Compounds containing condensed pyrimidine systems and a bridged nitrogen atom are known to present interest as potential analgetics, antitumor drugs, bronchial spasmolytics and breathing stimulants. They form the composition of some drugs. We studied the reaction of 2-(ethoxycarbonyl)methyl-1,4,6-trimethylpyrimidinium iodide with hydrazides of C-pyridyl-, C-pyrimidinyl-, N-azolyl- and C-pyrazolyl-substituted carboxylic acids. This reaction was shown to result in recyclization and formation of ethyl 2-(pyrimidinylalkyl)- and 2-(azolylalkyl)-5,7-dimethylpyrazolo[1,5-a]pyrimidine-3-carboxylates. It is a new rearrangement of 1,2-dialkylpyrimidinium salts proceeding through the pyrimidine ring recyclization with inclusion of the nucleophilic reagent fragment into the transformation product. Heterocyclic acids hydrazides, in which a hydrazide fragment is immediately connected with a heterocyclic ring, also undergo a similar reaction. By the reactions of salt 1 with isonicotinic acid hydrazide (isoniazid) and pyrazol-3-carboxylic acid hydrazide we managed to obtain pyrazolo[1,5-a] pyrimidine derivatives that contained in position 2 pyridine and pyrazole rings.Besides pyrazolopyrimidines, the separation of reaction mixture provided in some cases also another recyclization product, 2-hydroxy-5,7-dimethylpyrazolo[1,5-a] pyrimidine.

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