Synthesis of New Pharmacologically Active Piperidine-containing Polyheterocycles

Valentina K. Yu, K. D. Praliev, E. E. Fomicheva

Institute of Chemical Sciences of MS-AS RK, 106, Sh.Walihanov Str., Almaty, Kazakhstan,

Fax: 8-3272-615765, E-mail:adm@chem.academ.alma-ata.su

One of the selected directions of the investigations is the work on the study of some methods of the heterocyclization piperidones-4 in polycyclic systems containing the «pharmacophoric» piperidine cycle in the combination with the another heterocycles.

Spiroheterocyclic nitrogencontaining compounds are interest as the potential biological activity ones. The reaction of the number of N-alkoxyalkyl-3(H,Me)-piperidones-4 with the NaCN in the presence of ammonia carbonate in the mixture of ethanol-water is made in the soldered ampoules. After the neutralization by 3 % solution of chlorohydric acid the mixture of the reaction product with sodium chloride is obtained. The purification by the recrystallization from alcohol-water and another organic solvent mixtures did not give a good result. Therefore the obtained product was purified by elution of mixture of benzene with ethanol in different proportion on the column with aluminum oxide In the case of 3-methylpiperidones only one stereoisomer of spiropiperidinehigantoin was saturated in the both reaction. The configuration with the chair conformation of piperidine cycle having the equatorial 3-methyl group and the (C-4)-(NH) bond and the axial (C-4)-(C=O) bond was determined to each of both stereoisomers. This stereochemical result of Buherer-Bergs reaction was explained by the high stereodirection of nucleophilic addition of attacked reagent HCN to piperidone-4 carbonyl group (C=O), in this case 1-alkoxyalkyl-4a-cyan-4e-hydroxypiperidine with the conservation of equatorial orientation of 3-methyl group was obtained on the first reaction stage. The second stage - the replacement of hydroxy (OH) function to amino group carried out without the change of the C-4 center configuration. Then the hydrolysis with simultaneous intramolecular cyclization to hidantoin ring. The synthesized piperidinehidantoins had the high anesthetic activity more then one of lidocaine and novocaine in the experiments on frogs and guinea-pigs. These compounds were lowtoxic.

The simplicity of thiazoline derivatives synthesis at the Azinger's reaction conditions from alicyclic ketones having at any rate one alpha-hydrogen was served the main reason for the cycle of works on the study of piperidones-4 heterocyclization with elemental sulfur and gaseous ammonia. One of the synthesized piperidine-thiazolines had the high radioprotective action, besides, its spasmolitic activity was more then ones of no-shpa.

The obtained results of pharmacological tests showed the prospect of search of the new pharmacologically active substances in the number of bicycles, combining two different heterocycles in molecule, one of which was piperidine.

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