Synthesis of New Potential Analgesics from Phosphorylated Derivatives of benzo[e][1,4]diazepin-2-ones

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Benzodiazepine derivatives are promising compounds for treatment of nervous system disorders with wide spectrum of sedative, anxiolytic and myorelaxant action. Molecules of benzo[e][1,4]diazepin-2-ones are used in clinical setting. The aim of research project was synthesis of phosphorylated derivatives of 1,3-dihydro-2H-benzo[e][1,4]diazepin-2-one by the following reaction: interaction of 7-bromo-5-phenyl-1,3-dihydro-2H-benzo[e][1,4]diazepin-2-one with N-bromosuccinimide in glacial acetic acid; SR radical substitution to form intermediate, which reacted with sodium acetate to form the desired product that was further reacted with hydrazine to produce compound with hydroxyl group at the third position. Condensation of 7-bromo-3-hydroxy-5-(2-chlorophenyl)-1,3-dihydro-2H-benzo[e][1,4]diazepin-2-one in the presence of triethylamine with diphenylchlorophosfine obtaining 7-bromo-5-(2-chlorophenyl)-3-(diphenylphosphoryl)-1,3-dihydro-2H-benzo[e][1,4]diazepin-2-one that was previously unpublished in the literature. During the synthesis, a trivalent phosphorus intermediate undergoes Michaelis-Arbuzov reaction with two phosphorylated products at positions 3 and 5. Resulting molecule may show significant analgesic activity. The structures of the obtained molecules were identified with spectroscopy, NMR and Roentgen-structure analysis. Results: New variant of benzo[e][1,4]diazepin derivative 7-bromo-5-(2-chlorophenyl)-3-(diphenylphosphoryl)-1,3-dihydro-2H-benzo[e][1,4]diazepin-2-one belongs to undescribed 3-phosphorylated benzodiazepine is a potential analgesic compounds with low psychotropic activity. Synthesis mechanisms are described and possible interactions are discussed, molecular structure identified.

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