Full Paper _____ *Thematic Section:* Preparative Research.
The Reference Object Identifier – ROI: jbc-01/20-63-9-10 *Subsection:* Organic Chemistry.
The Digital Object Identifier – DOI: 10.37952/ROI-jbc-01/20-63-9-10
Submitted on September 20, 2020.

Synthesis of 3-arylisoxazoles and their sulfamide derivatives

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Keywords: isoxazoles, sulfonylchlorination, sulfonylamides, carboxamides, regioselectivity.

Abstract

Great interest in binuclear aromatic systems containing an isoxazole ring and a sulfamide group is due to the effect of two pharmacophore groups at once on the biological activity of these compounds. This article is devoted to the development of a method for the synthesis of 3-arylisoxazole-containing compounds and their sulfamide derivatives from simple and accessible products of organic synthesis. The target products of the developed multistage schemes are derivatives of various bicyclic systems containing an isoxazole ring and a second aromatic ring associated with a sulfofragment. The synthesis of 3-aryl-5-acylaminoisoxazoles was carried out by sequential conversion of methyl esters of aromatic carboxylic acids into the corresponding nitriles by reaction with acetonitrile in the presence of sodium hydride in dioxane. At the next stage, the nitriles reacted with hydroxylamine in an aqueous solution of sodium hydroxide to form the corresponding bicyclic amines, which were then acylated in acetonitrile with acetic acid chloride in the presence of pyridine. The total yields of 3-aryl-5-*N*-acylaminoisoxazoles were at least 60%. It was found that the sulfonylchlorination of 3-aryl-5-*N*-acylamino derivatives of isoxazole, depending on the experimental conditions and the structure of the starting substrates, forms both mono- and disulfochlorides. The regioselectivity of the sulfochlorination reaction of the synthesized bicyclic systems was proved by ^{1}H NMR spectroscopy. The influence of various factors on the course of the sulfochlorination reaction of the synthesized bicyclic systems was studied. The dependence of the direction of the electrophilic attack on the structure of the compounds and on the conditions of the experiment was established. As a result of the performed research, both mono and disulfochlorination products were obtained. With an increase in the reaction time, the disulfonylchlorination product accumulates and the deacylation reaction proceeds in parallel. Convincing proof of the structure of all synthesized compounds has been carried out using a complex of modern methods of physical and chemical analysis.

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