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LETTERS TO THE EDITOR

Dedicated to the 115th anniversary of B.A. Arbuzov's birth

Synthesis of Hybrid Pharmacophores Based on Adducts of *N*-Sulfinylaniline and Norbornadiene

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Abstract—Acylation of benzothiazinesulfonamides obtained by the oxidation of *N*-sulfinylaniline and norbornadiene adducts with acid chlorides and carboxylic anhydrides led to the formation of N-acylated sulfonamide hybrid pharmacophores. Molecular and crystal structure of the acylated products was established by X-ray diffraction method.

Keywords: sulfonamides, acylation, hybrid pharmacophores

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Sulfonamides have attracted considerable attention due to the wide spectrum of pharmacological activities, including antiviral, bactericidal, and others. Of particular interest are compounds with conjugated pharmacophore groups (sulfonamide, carbamide and etc.), as well as the formation of new pharmacophores based on sulfonamide species. Examples of these compounds are substances with an acylsulfonamide moiety that show antiviral activity against hepatitis C, like Asunaprevir [1], Danoprevir [2], Simeprevir [3], and their derivatives [4–6].

We attempted to acylate sulfonamides obtained by oxidizing adducts of *N*-sulfinylaniline and norbornadiene to obtain the corresponding *N*-acyl derivatives (Scheme 1). The compounds obtained contain an epoxy function with cytotoxic activity. Benzothiazinesulfonamide **1** was synthesized in accordance with the previously developed method through the Diels–Alder heteroatomic reaction [7]. The spectral characteristics of this compound have been reported in [7].

Acylation was carried out in two ways: by reaction with acid anhydrides (method *a*) and by reaction with acid chlorides in the presence of potassium carbonate (method *b*). The method *a* is simple, whereas method *b* is characterized by a short reaction time and availability of acylating agents.

The formation of *N*-acylated products **2–5** was indicated by the absence in the IR spectra of the N–H absorption band at 3270 cm^{-1}, as well as by the appearance of the absorption band in the 1710–1720 cm^{-1} region characteristic of the carbonyl group. In the ^1H NMR spectra of compounds **2–5** in addition to signals of the aromatic protons (7.15–7.30 ppm) and the bicyclo[2.2.1]heptamine fragment (1.25–3.50 ppm) there are also signals of the *N*-acyl fragment. The structure of compounds **2** and **3** was unambiguously confirmed by X-ray diffraction method (see the figure). X-Ray diffraction data of compounds **2** and **3** indicate the presence of the acetyl and propionyl groups at the nitrogen atom and the epoxy fragment in the molecule. The geometry of the norbornane fragment and the benzene ring in both structures is conventional. Thus, the annulation of the epoxy ring does not distort the bicyclic system of the norbonane fragment. The conformation of the central 6-membered heterocycle is a *semi-chair*; the C^{4A} and S^5 atoms are