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5-Amino-Substituted Derivatives of 4-Nitrofurazane: Synthesis, Structure, and Biological Activity

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Abstract—New amination reactions of 5-chloro-4-nitrobenzofurazane with different amines were studied. The reactions of 5-chloro-4-nitrobenzofurazane with 2,4,6-trichloro-, *para*-acetyl-, and *para*-carboxyethylanilines gave the products of aromatic nucleophilic substitution of the chlorine substituent in the nitrogenous heterocycle, the composition and structure of which was established by chemical, physical, and physicochemical methods and X-ray diffraction analysis. The thermal stability was studied by synchronous thermogravimetry and differential scanning calorimetry (TG–DSC). The synthesized compounds showed a high antibacterial and antimycotic activity against human and animal pathogenic microflora.

Keywords: substituted anilines, 5-chloro-4-nitrobenzofurazane, nucleophilic aromatic substitution, heterocyclic compounds

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Electrophilic–nucleophilic interactions are the most common processes in the synthetic organic chemistry of such nitrogenous heterocycles as substituted benzofurazanes and their oxides [1–10]. The methods for activation of aromatic heterocycles and, consequently, involvement them in nucleophilic aromatic substitution reactions are well known. The most used approach is the introduction of electron-acceptor substituents, for example, nitro groups, into such systems. 5-Chloro-4-nitrobenzofurazane is quite a reactive system containing an electrophilic benzofurazane ring which is prone to aromatic nucleophilic substitution (S_NAr) reactions due to the presence of an electron-acceptor substituent, specifically, nitro group. The amination of 5-chloro-4-nitrobenzofurazane with different amines occurs by the S_NAr mechanisms and leads to the products of aromatic nucleophilic substitution of the chlorine substituent in the six-membered ring with HCl elimination.

It is well known that substituted benzofurazanes and their oxides exhibit broad-range biological activity [1–5].

According to our previous findings gave unambiguous evidence showing that the reactions of dichlorodinitrobenzofuroxane and -furazane with different phosphines and amines in an alcohol–ether medium form exclusively the products of nucleophilic aromatic substitution of the Cl and NO_2 substituents in the nitrogenous heterocycle [6–10].

Aimed at extending the range of biologically active compounds, we reacted 5-chloro-4-nitrobenzo[*c*]-[1,2,5]oxadiazole **1** with such substituted anilines as *para*-acetyl-, *para*-carboxyethyl-, and 2,4,6-trichloroaniline in an ether–alcohol medium to synthesize the corresponding nucleophilic substitution products. The three reactions all gave monosubstituion products **3**, **5**, and **7**, respectively.

The reaction chloronitrobenzofurazane **1** with 2,4,6-trichloroaniline **2** at room temperature in a 1 : 3 ethanol–diethyl ether binary solvent resulted in the isolation of 4-nitro-*N*-(2,4,6-trichlorophenyl)benzo[*c*][1,2,5]oxadiazole-5-amine **3** (Scheme 1) as needle-like dark orange crystals, mp 138.4°C.

The composition and structure of the synthesized compound were confirmed by physical and physicochemical methods, including X-ray diffraction (XRD) analysis (Figs. 1 and 2). As seen from the figures, the trichlorophenylamino substituent in the aromatic ring of benzofurazane is orthogonal to the benzofurazane-ring plane due to steric strain.