SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 1,4-BENZOQUINONE 5-NITROFURAN-3-CARBOXAMIDRAZONES AND THEIR ACETYLATION PRODUCT

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The antibacterial properties of drugs belonging to the nitrofuran series are comparable with those of many antibiotics. Moreover, in some cases the former drugs are effective with respect to antibiotic-resistant forms of infection agents [1] and, in contrast to antibiotics, increase the general immune resistance of the macroorganism [2]. In continuation of the search for new effective antimicrobial nitrofuran-containing compounds, we have studied the reaction between 5-nitro-2-furancarbohydrazone acid and 1,4-benzoquinone leading to mono- and bisamidrazones (I, II). Taking into account that acetylation of similar amidrazones was known to increase their activity [3], we have also attempted to synthesize the acetyl derivatives of compound I and II. However, we failed to obtain the target compounds, because both systems featured detachment of the benzoquinone fragment with the formation of triazole (III). Similar transformations were described in [4, 5].

The synthesized compounds appear as substances of brown (I), dark-claret (II), or yellow (III) color, poorly soluble in most organic solvents.

The proposed structures were confirmed by the results of elemental analyses and the data of IR and 1H NMR spectroscopy.

EXPERIMENTAL CHEMICAL PART

The IR spectra were recorded on an UR-20 spectrophotometer (Germany) using samples prepared as nujol mulls. The ^{1}H NMR spectra were measured at room temperature with a Tesla BS-587A (80 MHz) spectrometer using DMSO-d_6 as the solvent and *tert*-BuOH as the internal standard.

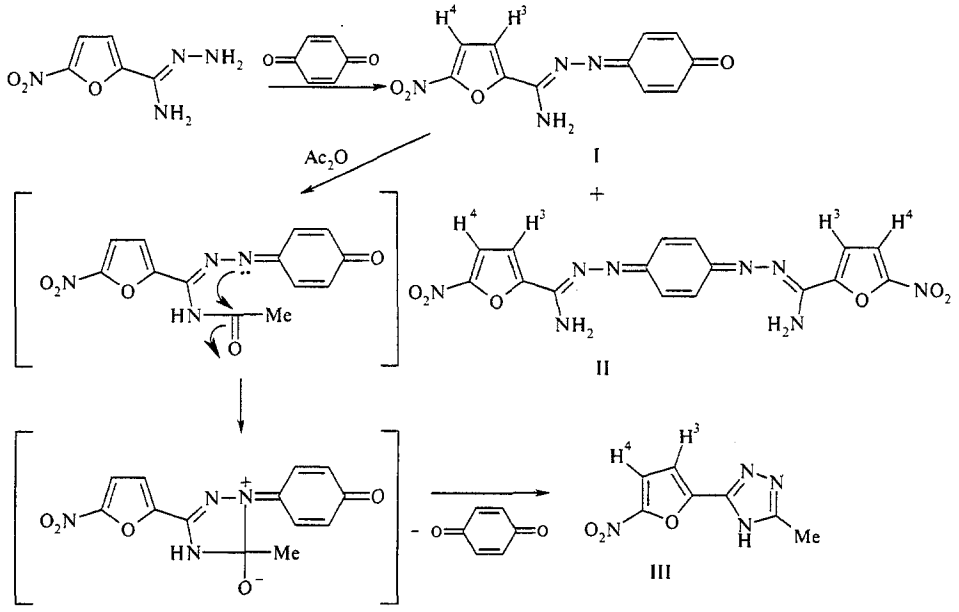

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TABLE 1. Antimicrobial Activity of Compounds I – III

Compound	MIC (μg/ml) with respect to	
	E. coli M-1749	St. aureus 209-P
I	6.25	3.13
II	1.56	3.13
III	6.25	1.56
Furagin	1.56	3.13

1-[3-(5-Nitro-2-furyl)amidrazono]-4-oxocyclohexa-2,5-diene (I). To 1.7 g (0.01 mole) of 5-nitro-2-furancarbohydrazone acid amide at 100°C was gradually (over 1 h) added 1.08 g (0.01 mole) of 1,4-benzoquinone in 20 ml dioxane. Then the reaction mixture was treated with 0.5 g of activated charcoal and filtered. The filtrate was poured by small portions with stirring into 150 ml of ice-cold water. The precipitated crystals were filtered and dried at room temperature. Yield of compound I, 2.0 g (85%); $C_{11}H_8N_4O_3$; ^{1}H NMR spectrum (δ, ppm): 6.61 (d, 1H, H^4), 6.31 (d, 1H, J 4.0 Hz, H^3), 5.68 (s, 2H, benzoquin.), 5.45 (s, 2H, benzoquin.).

1,4-Di[3-(5-Nitro-2-furyl)amidrazono]-4-oxocyclohexa-2,5-diene (II). To 3.4 g (0.02 mole) of 5-nitro-2-furancarbohydrazone acid amide at 100°C was gradually (over 1 h) added 1.08 g (0.01 mole) of 1,4-benzoquinone in 20 ml dioxane. Then the reaction mixture was treated as described above. Yield of compound II, 3.58 g (87%); $C_{16}H_{12}N_8O_6$; ^{1}H NMR spectrum (δ, ppm): 6.56 (d, 2H, H^4), 6.25 (d, 2H, J 4.0 Hz, H^3), 5.62 (s, 4H, benzoquin.).

3-Methyl-5-(5-nitro-2-furyl)-1,2,4-triazole (III). To 2.44 g (0.01 mole) of compound I at 120°C was gradually (over 1 h) added 30 ml of acetic anhydride, which was accompanied by precipitation of bright-yellow crystals. Then the reaction mixture was cooled and the precipitated crystals were filtered, washed with ethanol, and dried at room temperature. Yield of compound III, 1.82 g (94%); $C_7H_6N_4O_3$; ^{1}H NMR spectrum (δ, ppm): 9.20 (s, 1H, NH), 6.70 (d, 1H, H^4), 6.20 (d, 1H, J 4.0 Hz, H^3), 1.25 (s, 3H, CH_3).

The treatment of compound II under similar conditions also led to triazole III with a yield of 3.64 g (94%).

The antimicrobial activity of the synthesized compounds was studied by conventional methods [6]. The tests were performed with respect to the *Staphylococcus aureus* 209-R and *Escherichia coli* M-1749 strains. The antibacterial activity was estimated as the minimum inhibiting concentration (MIC) of the compound producing compete suppression of the test microbe growth under standard conditions. The reference compound was the drug furagin.

It was found that compounds I – III exhibit an antimicrobial effect comparable to that of furagin (Table 1).

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