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Reaction of *N*-Arenesulfonyl-1,4-benzoquinone Imines with Acetylacetone

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Abstract—*N*-Arenesulfonyl-1,4-benzoquinone imines reacted with acetylacetone to afford different products, depending on the isolation procedure. Crystallization from polar protic solvents gave *N*-[4-hydroxy-3-(2-hydroxy-4-oxopent-2-en-3-yl)phenyl]arenesulfonamides and 6-(2-oxopropyl)-4-(arenesulfonamido)phenyl acetates, whereas *N*-(3-acetyl-2,6-dimethyl-1-benzofuran-5-yl)arenesulfonamides were isolated by crystallization from nonpolar aprotic solvents.

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Benzofuran derivatives exhibit a broad spectrum of biological activity, in particular hypotensive, antianginal [1], antiarrhythmic [1, 2], analgesic, antispasmodic [3], local anesthetic [3, 4], anti-allergic [5], antimicrobial [6], and CNS activity [7]. Benzofuran derivatives were synthesized previously by reactions of CH acids with 1,4-benzoquinones [8–12] and *N*-(benzenesulfonyl)-1,4-benzoquinone imines [13, 14]. In most cases, the syntheses included several steps, one of which was treatment of intermediate products with inorganic acids [8–11, 13, 14] since the first step was 1,4-addition of CH acid to 1,4-benzoquinone or 1,4-benzoquinone imine. Martyak and Obushak [12] found conditions for one-step preparation of benzofurans from 2-aryl-1,4-benzoquinones, whereas we have revealed no published data on one-step synthesis of benzofuran derivatives from 1,4-benzoquinone imines. Furthermore, spectral characteristics of benzofuran derivatives obtained from *N*-benzenesulfonyl-1,4-benzoquinone imines were not reported.

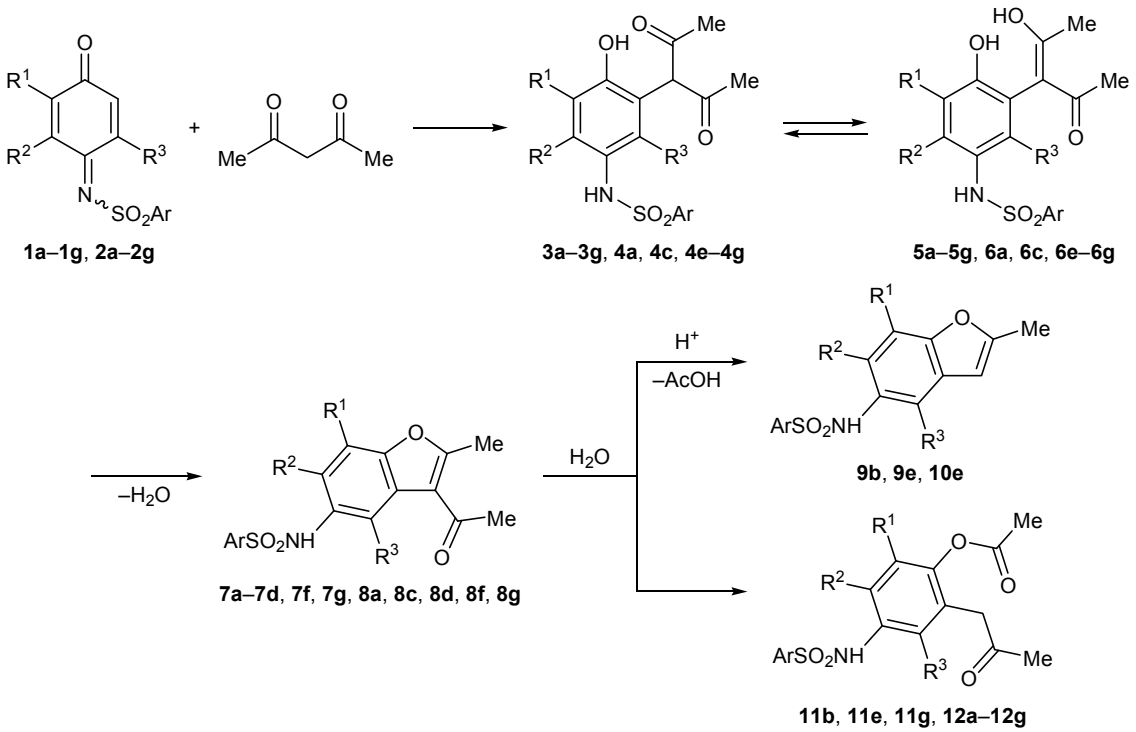
The goal of the present study was to find optimal conditions for the synthesis of benzofuran derivatives from *N*-arenesulfonyl-1,4-benzoquinone imines and acetylacetone. For this purpose, 1,4-benzoquinone imines **1a**–**1g** and **2a**–**2g** were reacted with acetylacetone in anhydrous dioxane in the presence of a catalytic amount of sodium methoxide. The solvent was removed, and the oily residue was treated with polar protic reagents or nonpolar aprotic solvent.

After treatment of the residue with water, we isolated 1,4-addition products for which keto–enol tautomerism is possible (**3** ⇄ **5**, **4** ⇄ **6**; Scheme 1). According to the ^{1}H NMR data, enol tautomers **5a**–**5g**, **6a**, **6c**, and **6e**–**6g** were present in solution. Prolonged treatment with water (24 h) led to the formation of compounds **11b**, **11e**, **11g**, and **12a**–**12g** via the transformation sequence **1** → **3** ⇄ **5** → **7** → **11** or **2** → **4** ⇄ **6** → **8** → **12**. These products result from irreversible opening of the furan ring in **7** and **8** through cleavage of the C^2=C^3 bond. Analogous products of C=C bond cleavage in benzofuran derivatives were isolated in the reactions of 2,3,5-trimethyl-1,4-benzoquinone with various CH acids [11].

Compounds **7a**–**7d**, **7f**, **7g**, **8a**, **8c**, **8d**, **8f**, and **8g** were synthesized in two ways. The first of these, as in the reactions with 1,4-benzoquinone [8–11], included two steps. 1,4-Addition products **5a**–**5g**, **6a**, **6c**, and **6e**–**6g** were treated with concentrated aqueous HCl on heating for 3 h under reflux. In some cases, prolonged treatment (6 h) gave compounds **9b**, **9e**, and **10e** in 51–56% yield.

In the second way, the oily residue obtained after removal of the solvent was treated with hexane, and benzofuran derivatives **7a**–**7d**, **7f**, **7g**, **8a**, **8c**, **8d**, **8f**, and **8g** crystallized from the hexane solution (yield 40–63%). Compounds **7** and **8** in acetone were converted into **11** and **12** in several days.

Scheme 1.



1, **3**, **5**, **7**, **9**, **11**, Ar = Ph; **2**, **4**, **6**, **8**, **10**, **12**, Ar = 4-MeC_6H_4; $R^1 = R^2 = R^3 = H$ (**a**); R^1 = Me, $R^2 = R^3 = H$ (**b**); $R^1 = R^3 = H$, R^2 = Me (**c**); $R^1 = R^2$ = Me, $R^3 = H$ (**d**); $R^1 = R^3$ = Me, $R^2 = H$ (**e**); $R^1 = H$, $R^2 = R^3$ = Me (**f**); R^1 = Cl, $R^2 = R^3 = H$ (**g**).

The structure of the synthesized compounds was confirmed by IR and ^1H and ^{13}C NMR spectra and elemental analyses. The ^1H NMR spectra of **5a**–**5g**, **6a**, **6c**, and **6e**–**6g** contained a singlet at δ 1.66–1.78 ppm from two methyl groups and a singlet at δ 16.73–16.79 ppm typical of enolic hydroxy proton. Compounds **7a**–**7d**, **7f**, **7g**, **8a**, **8c**, **8d**, **8f**, and **8g** showed in the ^1H NMR spectra a singlet at δ 2.38–2.55 ppm due to methyl group on C^2 and a singlet at δ 2.58–2.82 ppm due to acetyl group. In the ^1H NMR spectra of **9b**, **9e**, and **10e** we observed singlets at δ 2.40–2.42 (2-Me) and 6.40–6.50 ppm (3-H). Protons of the methylene group in **11b**, **11e**, **11g**, and **12a**–**12g** resonated in the ^1H NMR spectra in the region δ 3.45–3.66 ppm, and methyl proton signals of the $MeCOCH_2$ and MeCOO fragments were observed at δ 2.00–2.07 and 2.21–2.30 ppm, respectively.

The ^{13}C NMR spectra of **5b** and **5c** showed methyl carbon signals at δ_C 23.55–23.68 [C=C(OH)**Me**] and 23.60–23.75 ppm (**Me**CO) and signals at δ_C 109.66–110.10, 191.42–191.61, and 192.19–192.38 ppm from the **C**=C(OH)Me, C=**C**(OH)Me, and Me**C**O carbon atoms, respectively. Compound **12f** showed in the ^{13}C NMR spectrum signals at δ_C 21.42 (**Me**$COCH_2$), 29.17 (**Me**COO), 43.03 (CH_2), 186.04 (Me**C**OO), and 204.73 ppm (Me**C**OCH_2). In the IR spectra of **11b**, **11e**, **11g**, and **12a**–**12g**, absorption bands at 1750–1710 (ester carbonyl) and 3280 cm^{-1} (N–H) were observed.

The structure of **12c** and **12d** was determined by X-ray analysis (Figs. 1, 2). The independent part of a unit cell of **12d** contained two molecules **A** and **B** differing by some structural parameters. The C^{12}–C^{17} aromatic ring appears in *–sc* conformation with respect to the C^1–N^1 bond: the torsion angles $C^1N^1S^1C^{12}$ are –55.6(3)° (**12c**), –59.9(3)° (**12d**, **A**), and –63.6(3)° (**12d**, **B**); the torsion angles $N^1S^1C^{12}C^{13}$ (rotation about the S^1–N^1 bond) are 79.7(4)° (**12c**) and 91.4(2)° (**12d**, **A** and **B**). The tosyl substituent adopts *–sc* conformation about the C^1–C^6 bond in molecule **12c** and is orthogonal to that bond in **12d** [torsion angle $S^1N^1C^1C^6$ –59.2(3)° (**12c**), 92.7(3) (**12d**, **A**), 92.9(3)° (**12d**, **B**)]. Molecules **12c** and **12d** in crystal are linked through intramolecular hydrogen bonds N–H···O [**12c**: (–1 + *x*, *y*, *z*), H···O 2.02 Å, ∠NHO 156.4°; **12d**: (–1 + *x*, *y*, *z*), H···O 2.10 Å (**A**) 2.07 Å (**B**), ∠NHO 162.0° (**A**), 163.8° (**B**)] to form stacks along the [100] and [010] crystallographic directions, respectively.

Thus, we have proposed a fast one-step procedure for the synthesis of benzofuran derivatives from *N*-arenesulfonyl-1,4-benzoquinone imines and acetyl-

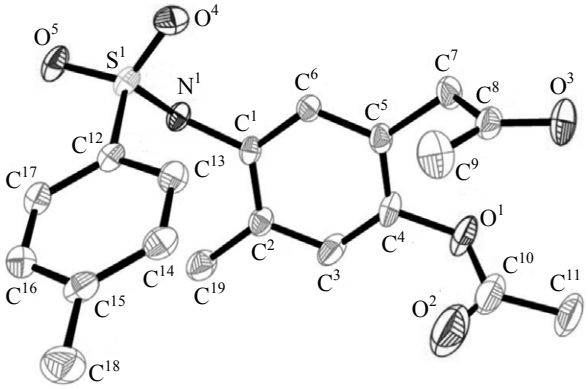


Fig. 1. Structure of the molecule of 5-methyl-4-(4-methylbenzenesulfonamido)-2-(2-oxopropyl)phenyl acetate (**12c**) according to the X-ray diffraction data.

acetone. Treatment of the addition products with polar solvents leads to opening of the furan ring with formation of compounds which, as well as benzofuran derivatives, are potentially biologically active.

PASS Online (Prediction of Activity Spectra for Substances) [15] analysis of possible biological activities of compounds **7a**–**7d**, **7f**, **7g**, **8a**, **8c**, **8d**, **8f**, **8g**, **9b**, **9e**, and **10e** revealed high probability for inhibition of glutamyl endopeptidase II (0.640–0.801), insulin-degrading enzyme (insulysin, 0.635–0.756), and ompT protease (omptin, 0.511–0.687). Compounds **11b**, **11e**, **11g**, and **12a**–**12g** were found to be potential inhibitors of gluconate 2-dehydrogenase (probability 0.802–0.823), glutamyl endopeptidase II (0.679–0.782), and ompT protease (0.596–0.714), as well as fibrinolytics (0.597–0.715) and antipyretics (0.453–0.657). It was also found that the presence of both donor and acceptor substituents in the initial 1,4-quinone imines reduces the probability of biological activity of products of their reaction with acetylacetone as compared to unsubstituted compounds **7a** and **8a**.

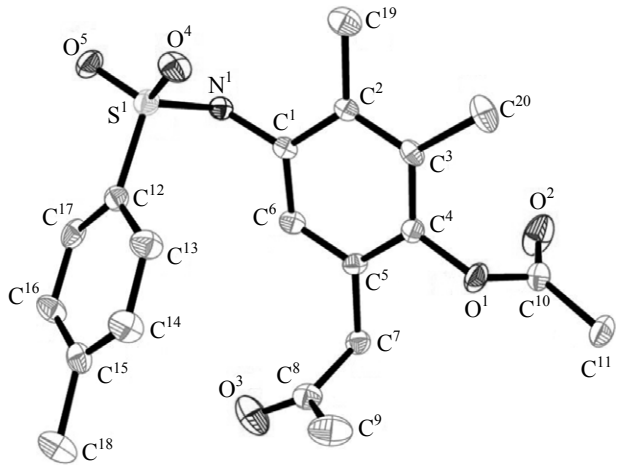


Fig. 2. Structure of the molecule of 2,3-dimethyl-4-(4-methylbenzenesulfonamido)-6-(2-oxopropyl)phenyl acetate (**12d**) according to the X-ray diffraction data.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer at 300 and 75.4 MHz, respectively, using acetone-d_6 as solvent and tetramethylsilane as internal standard. The purity of the initial quinone imines and isolated products was checked by TLC on Silufol UV-254 plates; quinone imines **1a**–**1g** and **2a**–**2g** were applied from solutions in chloroform, and benzene–hexane (10:1) was used as eluent; compounds **5**–**12** were applied from solutions in acetone, and ethanol–chloroform (1:10) was used as eluent; spots were detected under UV light.

The X-ray diffraction data for compounds **12c** and **12d** were obtained at 21°C on an Xcalibur-3 diffractometer (MoK_α radiation, CCD detector, graphite monochromator, ω-scanning, $2\theta_{max}$ = 50°). The structures were solved by the direct method using SHELXTL software package [16] and refined against F^2 by the full-matrix least-squares method in anisotropic approximation for non-hydrogen atoms. Hydrogen atoms were localized by difference synthesis of electron density, and their positions were refined according to the riding model ($U_{iso} = nU_{eq}$; n = 1.5 for methyl groups and n = 1.2 for other hydrogen atoms). The coordinates of atoms and complete tables of bond lengths and bond angles for structures **12c** and **12d** were deposited to the Cambridge Crystallographic Data Centre (entry nos. CCDC 1439271 and 1439272, respectively).

Compound **12c**. Triclinic crystal system, space group $P\bar{1}$; unit cell parameters: a = 9.7759(8), b = 10.3223(10), c = 11.0012(9) Å; α = 65.828(9), β = 72.329(7), γ = 75.656(8)°; V = 955.23(16) Å^3; M 375.43; Z = 2; d_{calc} = 1.305 g/cm^3; μ(MoK_α) = 0.198 mm^{-1}; F(000) = 396. Number of reflections 8226, including 4346 independent reflections (R_{int} = 0.0349). Final divergence factors R_1 = 0.066 [for 4346 reflections with $F > 4\sigma(F)$], wR_2 = 0.117 (for all 8226 reflections); goodness of fit S = 1.005.

Compound **12d**. Orthorhombic crystal system, space group $Pca2_1$; unit cell parameters: a = 20.4599(14), b = 5.2412(3), c = 36.669(3) Å; V = 3932.2(5) Å^3; M 389.45; Z = 8; d_{calc} = 1.316 g/cm^3, μ(MoK_α) = 0.195 mm^{-1}; F(000) = 1648. Number of reflections 34132; 8960 independent reflections (R_{int} =

0.1217). Final divergence factors R_1 = 0.084 [for 8960 reflections with $F > 4\sigma(F)$], wR_2 = 0.1742 (for all 34 132 reflections); goodness of fit S = 0.989.

Initial quinone imines **1a**–**1g** and **2a**–**2g** were synthesized according to the procedure described in [17]. Compounds **1a** [18, 19], **1b**, **1c**, **1g**, **2a** [19, 20], **2b**, **2c**, **2g** [19], **1d**, **2d** [21], **1e**, **1f**, **2e**, and **2f** [22] were reported previously.

Reaction of quinone imines 1a–1g and 2a–2g with acetylacetone (*general procedure***).** Sodium methoxide, 20 mg, was added under stirring to a solution of 2 mmol of quinone imine **1a**–**1g** or **2a**–**2g** and 2.2 mmol of acetylacetone in 25 mL of anhydrous dioxane. The solution turned colorless, the solvent was distilled off under reduced pressure, and the oily residue was treated as described below.

a. The oily residue was treated with water, the mixture was kept for 1 h, and the light brown crystalline solid was filtered off and recrystallized from ethanol or aqueous ethanol. We thus isolated pure compounds **5a**–**5f**, **6a**, **6c**, and **6f**, while compounds **5g**, **6e**, and **6g** were not isolated in the pure state.

b. The oily residue was treated with water, the mixture was kept for 24 h, and the light brown crystalline solid was filtered off and recrystallized from ethanol or aqueous ethanol. We thus isolated compounds **11b**, **11e**, **11g**, and **12a**–**12g**.

c. The oily residue was treated with hexane, and the mixture was kept for 24 h. The light brown crystalline residue was filtered off and recrystallized from ethanol. We thus isolated compounds **7b**, **7d**, **7g**, **8a**, **8d**, and **8g**.

Compounds 7a–7d, 7f, 7g, 8a, 8c, 8f, 8g, 9b, 9e, and 10e (*general procedure***).** A 10-mL round-bottom flask was charged with 1 mmol of **5a**–**5g**, **6a**, **6c**, or **6e**–**6g** and 5 mL of concentrated aqueous HCl, and the mixture was refluxed for 3 or 6 h. The dark brown crystalline solid was filtered off from the hot mixture and recrystallized from benzene. The product was compound **7a**–**7d**, **7f**, **7g**, **8a**, **8c**, **8f**, or **8g** (3 h) or **9b**, **9e**, or **10e** (6 h).

***N*-[4-Hydroxy-3-(2-hydroxy-4-oxopent-2-en-3-yl)phenyl]benzenesulfonamide (5a).** Yield 83%, mp 169–170°C. ^{1}H NMR spectrum, δ, ppm: 1.72 s (6H, Me), 6.82 d (1H, 2-H, J = 3.0 Hz), 6.87 d (1H, 5-H, J = 6.0 Hz), 7.09 d.d (1H, 6-H, J = 3.0, 6.0 Hz), 7.51–7.73 m (5H, Ph), 8.35 br.s (1H, NH), 8.66 s (1H, OH), 16.75 s (1H, OH). Found, %: N 3.93; S 8.96. $C_{17}H_{17}NO_5S$. Calculated, %: N 4.00; S 9.21.

***N*-[4-Hydroxy-3-(2-hydroxy-4-oxopent-2-en-3-yl)-5-methylphenyl]benzenesulfonamide (5b).** Yield 89%, mp 188–189°C. ^{1}H NMR spectrum, δ, ppm: 1.70 s (6H, Me), 2.19 s (3H, 5-Me), 6.63 d (1H, 6-H, J = 2.7 Hz), 7.02 d (1H, 2-H, J = 2.7 Hz), 7.51–7.73 m (5H, Ph), 8.58 br.s (1H, NH), 16.77 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 16.56 (5-Me), 23.55 [C=C(OH)**C**H$_3$], 23.60 (CO**C**H$_3$), 109.66 [**C**=C(OH)Me], 123.61 (C^3), 125.38 (C^2), 126.55 (C^5), 127.00 (C^6), 127.97 (C^o), 129.55 (C^m), 129.86 (C^1), 133.21 (C^p), 140.49 (C^i), 152.06 (C^4), 191.61 [C=**C**(OH)Me], 192.38 (Me**C**O). Found, %: N 4.31; S 9.02. $C_{18}H_{19}NO_5S$. Calculated, %: N 3.88; S 8.86.

***N*-[4-Hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)-2-methylphenyl]benzenesulfonamide (5c).** Yield 87%, mp 196°C. ^{1}H NMR spectrum, δ, ppm: 1.78 s (6H, Me), 2.09 s (3H, 2-Me), 6.67 s (1H, 3-H), 6.77 s (1H, 6-H), 7.52–7.72 m (5H, Ph), 8.31 s (1H, NH), 16.75 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 18.07 (2-Me), 23.68 [C=C(OH)**C**H$_3$], 23.75 (CO**C**H$_3$), 110.10 [**C**=C(OH)Me], 118.60 (C^6), 127.66 (C^5), 128.09 (C^o), 129.83 (C^m), 129.92 (C^1), 132.77 (C^3), 133.42 (C^p), 138.14 (C^2), 141.52 (C^i), 155.06 (C^4), 191.42 [C=**C**(OH)Me], 192.19 (Me**C**O). Found, %: N 3.84; S 8.90. $C_{18}H_{19}NO_5S$. Calculated, %: N 3.88; S 8.86.

***N*-[4-Hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)-2,3-dimethylphenyl]benzenesulfonamide (5d).** Yield 91%, mp 174°C. ^{1}H NMR spectrum, δ, ppm: 1.73 s (6H, Me), 2.12 s (3H, 3-Me), 2.17 s (3H, 2-Me), 6.45 s (1H, 6-H), 7.50–7.71 m (5H, Ph), 8.25 br.s (1H, NH), 16.77 s (1H, OH). Found, %: N 3.56; S 8.49. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

***N*-[4-Hydroxy-3-(2-hydroxy-4-oxopent-2-en-3-yl)-2,5-dimethylphenyl]benzenesulfonamide (5e).** Yield 83%, mp 177–179°C. ^{1}H NMR spectrum, δ, ppm: 1.72 s (6H, Me), 2.11 s (3H, 5-Me), 2.17 s (3H, 2-Me), 6.78 s (1H, 6-H), 7.50–7.71 m (5H, Ph), 8.10 br.s (1H, NH), 16.77 s (1H, OH). Found, %: N 3.56; S 8.49. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

***N*-[4-Hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)-2,6-dimethylphenyl]benzenesulfonamide (5f).** Yield 84%, mp 199°C. ^{1}H NMR spectrum, δ, ppm: 1.69 s (3H, 6-Me), 1.74 s (6H, Me), 2.10 s (3H, 2-Me), 6.71 s (1H, 3-H), 7.54–7.72 m (5H, Ph), 8.14 br.s (1H, NH), 16.74 s (1H, OH). Found, %: N 3.80; S 8.59. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

***N*-[3-Chloro-4-hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)phenyl]benzenesulfonamide (5g).** ^{1}H NMR

spectrum, δ, ppm: 1.72 s (6H, Me), 6.83 d (1H, 6-H, *J* = 2.4 Hz), 7.26 d (1H, 2-H, *J* = 2.7 Hz), 7.53–7.79 m (5H, Ph), 8.85 br.s (1H, NH), 16.77 s (1H, OH). Found, %: N 3.73; S 8.47. $C_{17}H_{16}NO_5S$. Calculated, %: N 3.67; S 8.38.

***N*-[4-Hydroxy-3-(2-hydroxy-4-oxopent-2-en-3-yl)phenyl]-4-methylbenzenesulfonamide (6a).** Yield 84%, mp 169–171°C. ^{1}H NMR spectrum, δ, ppm: 1.70 s (6H, Me), 2.34 s (3H, 4′-CH_3), 6.79 d (1H, 2-H, *J* = 3.0 Hz), 6.85 d (1H, 5-H, *J* = 6.0 Hz), 7.07 d.d (1H, 6-H, *J* = 3.0, 6.0 Hz), 7.29 d (2H, 3′-H, 5′-H, *J* = 9.0 Hz), 7.57 d (2H, 2′-H, 6′-H, *J* = 9.0 Hz), 8.54 s (1H, NH), 16.73 s (1H, OH). Found, %: N 4.27; S 8.92. $C_{18}H_{19}NO_5S$. Calculated, %: N 3.88; S 8.86.

***N*-[4-Hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)-2-methylphenyl]-4-methylbenzenesulfonamide (6c).** Yield 87%, mp 169–170°C. ^{1}H NMR spectrum, δ, ppm: 1.77 s (6H, Me), 2.09 s (3H, 2-Me), 2.40 s (3H, 4′-CH_3), 6.68 s (1H, 3-H), 6.77 s (1H, 6-H), 7.35 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.59 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 8.31 s (1H, NH), 16.76 s (1H, OH). Found, %: N 3.79; S 8.56. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

***N*-[4-Hydroxy-3-(2-hydroxy-4-oxopent-2-en-3-yl)-2,5-dimethylphenyl]-4-methylbenzenesulfonamide (6e).** ^{1}H NMR spectrum, δ, ppm: 1.64 s (3H, 5-Me), 1.66 s (6H, Me), 2.18 s (3H, 2-Me), 2.39 s (3H, 4′-CH_3), 6.77 s (1H, 6-H), 7.33 d (2H, 3′-H, 5′-H, *J* = 6.0 Hz), 7.53 d (2H, 2′-H, 6′-H, *J* = 6.0 Hz), 8.11 br.s (1H, NH), 16.79 s (1H, OH). Found, %: N 3.62; S 8.25. $C_{20}H_{23}NO_5S$. Calculated, %: N 3.59; S 8.22.

***N*-[4-Hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)-2,6-dimethylphenyl]-4-methylbenzenesulfonamide (6f).** Yield 85%, mp 184°C. ^{1}H NMR spectrum, δ, ppm: 1.70 s (3H, 6-Me), 1.73 s (6H, Me), 2.10 s (3H, 2-Me), 2.41 s (3H, 4′-CH_3), 6.69 s (1H, 3-H), 7.35 d (2H, 3′-H, 5′-H, *J* = 7.8 Hz), 7.58 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 8.00 br.s (1H, NH), 16.75 s (1H, OH). Found, %: N 3.65; S 8.29. $C_{20}H_{23}NO_5S$. Calculated, %: N 3.59; S 8.22.

***N*-[3-Chloro-4-hydroxy-5-(2-hydroxy-4-oxopent-2-en-3-yl)phenyl]-4-methylbenzenesulfonamide (6g).** ^{1}H NMR spectrum, δ, ppm: 1.71 s (6H, Me), 2.35 s (3H, 4′-CH_3), 6.82 s (1H, 2-H, *J* = 2.1 Hz), 7.26 m.d (1H, 6-H, *J* = 2.7 Hz), 7.33 d (2H, 3′-H, 5′-H, *J* = 7.8 Hz), 7.61 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 8.36 br.s (1H, NH), 16.77 s (1H, OH). Found, %: N 3.66; S 8.42. $C_{18}H_{18}NO_5S$. Calculated, %: N 3.54; S 8.09.

***N*-(3-Acetyl-2-methyl-1-benzofuran-5-yl)benzenesulfonamide (7a).** Yield 54%, mp 191°C. ^{1}H NMR spectrum, δ, ppm: 2.51 s (3H, 2-Me), 2.74 s (3H, MeCO), 7.19 d.d (1H, 6-H, *J* = 3.0, 9.0 Hz), 7.39 d (1H, 7-H, *J* = 9.0 Hz), 7.48–7.78 m (5H, Ph), 7.86 d (1H, 4-H, *J* = 3.0 Hz), 8.98 s (1H, NH). Found, %: N 4.36; S 9.81. $C_{17}H_{15}NO_4S$. Calculated, %: N 4.25; S 9.72.

***N*-(3-Acetyl-2,7-dimethyl-1-benzofuran-5-yl)-benzenesulfonamide (7b).** Yield 61%, mp 223°C. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, 7-Me), 2.49 s (3H, 2-Me), 2.74 s (3H, MeCO), 7.02 d (1H, 6-H, *J* = 0.9 Hz), 7.48–7.78 m (5H, Ph), 7.66 d (1H, 4-H, *J* = 0.9 Hz), 8.89 br.s (1H, NH). Found, %: N 3.89; S 9.17. $C_{18}H_{17}NO_4S$. Calculated, %: N 4.08; S 9.32.

***N*-(3-Acetyl-2,6-dimethyl-1-benzofuran-5-yl)-benzenesulfonamide (7c).** Yield 58%, mp 200–202°C. ^{1}H NMR spectrum, δ, ppm: 2.22 s (3H, 6-Me), 2.44 s (3H, 2-Me), 2.74 s (3H, MeCO), 7.34 s (1H, 7-H), 7.52–7.73 m (5H, Ph), 7.57 s (1H, 4-H), 8.40 br.s (1H, NH). Found, %: N 4.26; S 9.47. $C_{18}H_{17}NO_4S$. Calculated, %: N 4.08; S 9.32.

***N*-(3-Acetyl-2,6,7-trimethyl-1-benzofuran-5-yl)-benzenesulfonamide (7d).** Yield 61%, mp 208–210°C. ^{1}H NMR spectrum, δ, ppm: 2.18 s (3H, 6-Me), 2.37 s (3H, 7-Me), 2.38 s (3H, 2-Me), 2.75 s (3H, MeCO), 7.39 s (1H, 4-H), 7.51–7.72 m (5H, Ph), 8.42 br.s (1H, NH). Found, %: N 3.87; S 8.88. $C_{19}H_{19}NO_4S$. Calculated, %: N 3.92; S 8.96.

***N*-(3-Acetyl-2,4,6-trimethyl-1-benzofuran-5-yl)-benzenesulfonamide (7f).** Yield 56%, mp 199°C. ^{1}H NMR spectrum, δ, ppm: 2.10 s (3H, 4-Me), 2.14 s (3H, 6-Me), 2.50 s (3H, 2-Me), 2.58 s (3H, MeCO), 7.16 s (1H, 7-H), 7.52–7.72 m (5H, Ph), 8.24 br.s (1H, NH). Found, %: N 4.01; S 9.03. $C_{19}H_{19}NO_4S$. Calculated, %: N 3.92; S 8.96.

***N*-(3-Acetyl-7-chloro-2-methyl-1-benzofuran-5-yl)benzenesulfonamide (7g).** Yield 59%, mp 213°C. ^{1}H NMR spectrum, δ, ppm: 2.55 s (3H, 2-Me), 2.82 s (3H, MeCO), 7.29 d (1H, 6-H, *J* = 1.8 Hz), 7.50–7.82 m (5H, Ph), 7.85 d (1H, 4-H, *J* = 1.8 Hz), 9.16 br.s (1H, NH). Found, %: N 3.77; S 8.63. $C_{17}H_{14}ClNO_4S$. Calculated, %: N 3.85; S 8.80.

***N*-(3-Acetyl-2-methyl-1-benzofuran-5-yl)-4-methylbenzenesulfonamide (8a).** Yield 57%, mp 229°C. ^{1}H NMR spectrum, δ, ppm: 2.33 s (3H, 4′-CH_3), 2.52 s (3H, 2-Me), 2.75 s (3H, MeCO), 7.19 q (1H, 5-H, *J* = 3.0, 9.0 Hz), 7.28 d (2H, 3′-H, 5′-H, *J* = 9.0 Hz), 7.39 d (1H, 7-H, *J* = 9.0 Hz), 7.65 d (2H, 2′-H, 6′-H, *J* = 9.0 Hz), 7.86 d (1H, 4-H, *J* = 3.0 Hz),

8.91 s (1H, NH). Found, %: N 3.92; S 8.99. $C_{18}H_{17}NO_4S$. Calculated, %: N 4.08; S 9.32.

***N*-(3-Acetyl-2,6-dimethyl-1-benzofuran-5-yl)-4-methylbenzenesulfonamide (8c).** Yield 59%, mp 189°C. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H, 6-Me), 2.40 s (3H, 4′-CH_3), 2.44 s (3H, 2-Me), 2.74 s (3H, MeCO), 7.35 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.36 s (1H, 7-H), 7.60 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 7.64 s (1H, 4-H), 8.34 br.s (1H, NH). Found, %: N 4.00; S 9.12. $C_{19}H_{19}NO_4S$. Calculated, %: N 3.92; S 8.96.

***N*-(3-Acetyl-2,6,7-trimethyl-1-benzofuran-5-yl)-4-methylbenzenesulfonamide (8d).** Yield 63%, mp 181–182°C. ^{1}H NMR spectrum, δ, ppm: 2.18 s (3H, 6-Me), 2.35 s (3H, 4′-CH_3), 2.36 s (3H, 7-Me), 2.39 s (3H, 2-Me), 2.72 s (3H, MeCO), 7.33 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.34 s (1H, 4-H), 7.57 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 8.31 br.s (1H, NH). Found, %: N 3.85; S 8.73. $C_{20}H_{21}NO_4S$. Calculated, %: N 3.77; S 8.62.

***N*-(3-Acetyl-2,4,6-trimethyl-1-benzofuran-5-yl)-4-methylbenzenesulfonamide (8f).** Yield 40%, mp 134–135°C. ^{1}H NMR spectrum, δ, ppm: 2.12 s (3H, 4-Me), 2.16 s (3H, 6-Me), 2.42 s (3H, 4′-CH_3), 2.51 s (3H, 2-Me), 2.59 s (3H, MeCO), 7.16 s (1H, 7-H), 7.36 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.59 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 8.16 s (1H, NH). Found, %: N 3.84; S 8.70. $C_{20}H_{21}NO_4S$. Calculated, %: N 3.77; S 8.62.

***N*-(3-Acetyl-7-chloro-2-methyl-1-benzofuran-5-yl)-4-methylbenzenesulfonamide (8g).** Yield 59%, mp 248°C. ^{1}H NMR spectrum, δ, ppm: 2.33 s (3H, 4′-CH_3), 2.54 s (3H, 2-Me), 2.81 s (3H, MeCO), 7.28 d (1H, 6-H, *J* = 2.1 Hz), 7.31 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.68 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz), 7.84 d (1H, 4-H, *J* = 2.1 Hz), 9.09 br.s (1H, NH). Found, %: N 3.63; S 8.21. $C_{18}H_{16}ClNO_4S$. Calculated, %: N 3.70; S 8.47.

***N*-(2,7-Dimethyl-1-benzofuran-5-yl)benzenesulfonamide (9b).** Yield 56%, mp 112–113°C. ^{1}H NMR spectrum, δ, ppm: 2.34 s (3H, 7-Me), 2.40 s (3H, 2-Me), 6.40 s (1H, 3-H), 6.85 br.s (1H, 6-H), 7.13 d (1H, 4-H, *J* = 2.1 Hz), 7.45–7.75 m (5H, Ph), 8.79 br.s (1H, NH). Found, %: N 4.89; S 10.97. $C_{16}H_{15}NO_3S$. Calculated, %: N 4.65; S 10.62.

***N*-(2,4,7-Trimethyl-1-benzofuran-5-yl)benzenesulfonamide (9e).** Yield 51%, mp 114°C. ^{1}H NMR spectrum, δ, ppm: 2.17 s (3H, 4-Me), 2.30 s (3H, 7-Me), 2.42 s (3H, 2-Me), 6.50 s (1H, 3-H), 6.72 s (1H, 6-H), 7.50–7.69 m (5H, Ph), 8.34 br.s (1H, NH). Found, %: N 4.12; S 9.97. $C_{17}H_{17}NO_3S$. Calculated, %: N 4.44; S 10.15.

4-Methyl-*N*-(2,4,7-trimethylbenzofuran-5-yl)-benzenesulfonamide (10e). Yield 54%, mp 125°C. ^{1}H NMR spectrum, δ, ppm: 2.10 s (3H, 4-Me), 2.30 s (3H, 7-Me), 2.38 s (3H, 4′-CH_3), 2.42 s (3H, 2-Me), 6.44 s (1H, 3-H), 6.75 s (1H, 6-H), 7.29 d (2H, 3′-H, 5′-H, *J* = 7.8 Hz), 7.53 d (2H, 2′-H, 6′-H, *J* = 7.8 Hz), 8.21 br.s (1H, NH). Found, %: N 4.37; S 9.92. $C_{18}H_{19}NO_3S$. Calculated, %: N 4.25; S 9.72.

4-(Benzenesulfonamido)-2-methyl-6-(2-oxopropyl)phenyl acetate (11b). Yield 86%, mp 175–176°C. ^{1}H NMR spectrum, δ, ppm: 1.96 s (3H, 2-Me), 2.02 s (3H, **Me**$COCH_2$), 2.23 s (3H, MeCOO), 3.57 s (2H, CH_2), 7.00 d (1H, 3-H, *J* = 0.6 Hz), 7.17 br.s (1H, 5-H), 7.49–7.76 m (5H, Ph), 8.51 br.s (1H, NH). Found, %: N 3.96; S 9.01. $C_{18}H_{19}NO_5S$. Calculated, %: N 3.88; S 8.86.

4-(Benzenesulfonamido)-3,6-dimethyl-2-(2-oxopropyl)phenyl acetate (11e). Yield 84%, mp 165–166°C. ^{1}H NMR spectrum, δ, ppm: 1.90 s (3H, 3-Me), 2.01 s (3H, 6-Me), 2.02 s (3H, **Me**$COCH_2$), 2.30 s (3H, MeCOO), 3.63 s (2H, CH_2), 6.94 s (1H, 5-H), 7.51–7.70 m (5H, Ph), 8.37 br.s (1H, NH). Found, %: N 3.59; S 8.37. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

4-(Benzenesulfonamido)-2-chloro-6-(2-oxopropyl)phenyl acetate (11g). Yield 87%, mp 155–156°C. ^{1}H NMR spectrum, δ, ppm: 2.07 s (3H, **Me**$COCH_2$), 2.30 s (3H, MeCOO), 3.66 s (2H, CH_2), 6.95 d (1H, 3-H, *J* = 2.7 Hz), 7.16 d (1H, 5-H, *J* = 2.7 Hz), 7.53–7.79 m (5H, Ph), 8.80 br.s (1H, NH). Found, %: N 3.42; S 7.95. $C_{17}H_{16}ClNO_5S$. Calculated, %: N 3.67; S 8.38.

4-(4-Methylbenzenesulfonamido)-2-(2-oxopropyl)phenyl acetate (12a). Yield 83%, mp 123°C. ^{1}H NMR spectrum, δ, ppm: 2.03 s (3H, **Me**$COCH_2$), 2.25 s (3H, MeCOO), 2.37 s (3H, 4′-CH_3), 3.51 s (2H, CH_2), 6.96 br.s (2H, 3-H, 5-H), 7.02 br.s (1H, 6-H), 7.22 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.65 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz). Found, %: N 3.65; S 8.71. $C_{18}H_{19}NO_5S$. Calculated, %: N 3.88; S 8.86.

2-Methyl-(4-methylbenzenesulfonamido)-6-(2-oxopropyl)phenyl acetate (12b). Yield 87%, mp 131–132°C. ^{1}H NMR spectrum, δ, ppm: 1.96 s (3H, 2-Me), 2.02 s (3H, **Me**$COCH_2$), 2.23 s (3H, MeCOO), 2.34 s (3H, 4′-CH_3), 3.51 s (2H, CH_2), 7.01 d (2H, 3-H, 5-H, *J* = 6.0 Hz), 7.31 d (2H, 3′-H, 5′-H, *J* = 8.1 Hz), 7.69 d (2H, 2′-H, 6′-H, *J* = 8.1 Hz). Found, %: N 3.85; S 8.61. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

5-Methyl-4-(4-methylbenzenesulfonamido)-2-(2-oxopropyl)phenyl acetate (12c). Yield 86%, mp 127–128°C. ^{1}H NMR spectrum, δ, ppm: 2.02 s (3H, **Me**COCH$_2$), 2.05 s (3H, 5-Me), 2.21 s (3H, MeCOO), 2.39 s (3H, 4′-CH$_3$), 3.56 s (2H, CH$_2$), 6.92 s (1H, 6-H), 7.10 s (1H, 3-H), 7.33 d (2H, 3′-H, 5′-H, J = 8.1 Hz), 7.60 d (2H, 2′-H, 6′-H, J = 8.1 Hz), 8.36 br.s (1H, NH). Found, %: N 3.59; S 8.39. $C_{19}H_{21}NO_5S$. Calculated, %: N 3.73; S 8.53.

2,3-Dimethyl-4-(4-methylbenzenesulfonamido)-6-(2-oxopropyl)phenyl acetate (12d). Yield 92%, mp 158°C. ^{1}H NMR spectrum, δ, ppm: 1.95 s (3H, 2-Me), 1.99 s (3H, 3-Me), 2.06 s (3H, **Me**COCH$_2$), 2.28 s (3H, MeCOO), 2.40 s (3H, 4′-CH$_3$), 3.45 s (2H, CH$_2$), 6.86 s (1H, 5-H), 7.34 d (2H, 3′-H, 5′-H, J = 7.8 Hz), 7.59 d (2H, 2′-H, 6′-H, J = 7.8 Hz), 8.33 br.s (1H, NH). Found, %: N 3.48; S 8.01. $C_{20}H_{23}NO_5S$. Calculated, %: N 3.60; S 8.22.

3,6-Dimethyl-4-(4-methylbenzenesulfonamido)-2-(2-oxopropyl)phenyl acetate (12e). Yield 84%, mp 138–139°C. ^{1}H NMR spectrum, δ, ppm: 1.90 s (3H, 3-Me), 2.00 s (3H, 6-Me), 2.00 s (3H, **Me**COCH$_2$), 2.28 s (3H, MeCOO), 2.37 s (3H, 4′-CH$_3$), 3.61 s (2H, CH$_2$), 6.94 s (1H, 5-H), 7.32 d (2H, 3′-H, 5′-H, J = 7.8 Hz), 7.55 d (2H, 2′-H, 6′-H, J = 7.8 Hz), 8.27 br.s (1H, NH). Found, %: N 3.83; S 8.51. $C_{20}H_{23}NO_5S$. Calculated, %: N 3.60; S 8.22.

3,5-Dimethyl-4-(4-methylbenzenesulfonamido)-2-(2-oxopropyl)phenyl acetate (12f). Yield 85%, mp 163°C. ^{1}H NMR spectrum, δ, ppm: 1.93 s (3H, 5-Me), 2.04 s (3H, 3-Me), 2.06 s (3H, **Me**COCH$_2$), 2.25 s (3H, MeCOO), 2.42 s (3H, 4′-CH$_3$), 3.65 s (2H, CH$_2$), 6.84 s (1H, 6-H), 7.36 d (2H, 3′-H, 5′-H, J = 8.1 Hz), 7.59 d (2H, 2′-H, 6′-H, J = 8.1 Hz), 8.15 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 16.19 (4′-CH$_3$), 19.09 (5-Me), 20.84 (3-Me), 21.42 (**Me**COCH$_2$), 29.17 (**Me**COO), 43.03 (CH$_2$), 122.80 (C^6), 126.33 (C^5), 127.89 (C$^{2'}$, C$^{6'}$), 130.45 (C$^{3'}$, C$^{5'}$), 132.20 (C^4), 138.75 (C^2), 139.99 (C$^{1'}$), 144.18 (C^3), 149.39 (C$^{4'}$), 169.43 (C^1), 186.04 (Me**C**OO), 204.73 (Me**C**OCH$_2$). Found, %: N 3.52; S 7.98. $C_{20}H_{23}NO_5S$. Calculated, %: N 3.60; S 8.22.

4-(4-Methylbenzenesulfonamido)-2-chloro-6-(2-oxopropyl)phenyl acetate (12g). Yield 89%, mp 143–144°C. ^{1}H NMR spectrum, δ, ppm: 2.02 s (3H, **Me**COCH$_2$), 2.27 s (3H, MeCOO), 2.30 s (3H, 4′-CH$_3$), 3.66 s (2H, CH$_2$), 6.95 d (1H, 3-H, J = 2.4 Hz), 7.16 d (1H, 5-H, J = 1.8 Hz), 7.33 d (2H, 3′-H, 5′-H, J = 8.1 Hz), 7.61 d (2H, 2′-H, 6′-H, J = 8.1 Hz), 9.32 s (1H, NH). Found, %: N 3.36; S 8.18. $C_{18}H_{18}ClNO_5S$. Calculated, %: N 3.54; S 8.09.

REFERENCES

1. Kadieva, M.G., Oganesyan, E.T., Abaev, V.T., Butin, A.V., Gutnov, A.V., and Ivashev, M.N., RU Patent no. 2138492, 1997.
2. Druzgala, P., RU Patent 2373199, 2005; *Byull. Izobret*., 2009, no. 32; Druzgala, P., US Patent no. 5364880, 2005.
3. Mashkovskii, M.D., *Lekarstva XX veka* (XXth Century Drugs), Moscow: Novaya Volna, 1998, p. 239.
4. Grinev, A.N., Zotova, S.A., Stolyarchyk, A.A., Gaevoi, B.P., and Matsak, B.B., *Pharm. Chem. J*., 1979, vol. 13, no. 1, p. 44.
5. Atkinson, J.G., Guindon, Y., and Lau, S.K., US Patent no. 4663347, 1985; *Ref. Zh., Khim*., 1988, no. 3O90P.
6. Grinev, A.N., Zotova, S.A., Mikhailova, I.H., Stolyarchyk, A.A., Stepanyuk, G.I., Matsak, B.B., Sizova, T.N., and Pershin, G.N., *Pharm. Chem. J*., 1979, vol. 13, no. 8, p. 814.
7. Bathe, A., Helfert, B., and Böttcher, H., RU Patent no. 2278862, 2000; *Byull. Izobret*., 2006, no. 18.
8. Ionescu, M.V., *Bull. Soc. Chim. Fr*., 1927, vol. 41, p. 1094.
9. Smith, L.I. and MacMullen, C.W., *J. Am. Chem. Soc*., 1936, vol. 58, p. 629.
10. Smith, L.I. and Dale, W.J., *J. Org. Chem*., 1950, vol. 15, p. 832.
11. Smith, L.I. and Kaiser, E.W., *J. Am. Chem. Soc*., 1940, vol. 62, p. 133.
12. Martyak, R. and Obushak, M., *Visnik L'viv. Univ., Ser. Khim*., 2008, no. 49, part 2, p. 81.
13. Adams, R. and Whitaker, L., *J. Am. Chem. Soc*., 1956, vol. 78, p. 658.
14. Adams, R. and Reifschneider, W., *Bull. Soc. Chim. Fr*., 1958, no. 1, p. 23.
15. Filimonov, D.A., Lagunin, A.A., Gloriozova, T.A., Rudik, A.V., Druzhilovskii, D.S., Pogodin, P.V., and Poroikov, V.V., *Chem. Heterocycl. Compd*., 2014, vol. 50, no. 3, p. 444.
16. Sheldrick, G.M., *Acta Crystallogr., Sect. A*, 2015, vol. 71, p. 3.
17. Adams, R. and Nagarkatti, A., *J. Am. Chem. Soc*., 1950, vol. 72, p. 4601.
18. Burmistrov, S.I. and Titov, E.A., *Zh. Obshch. Khim*., 1952, vol. 22, p. 999.
19. Avdeenko, A.P. and Konovalova, S.A., *Russ. J. Org. Chem*., 2006, vol. 42, p. 349.
20. Adams, R. and Looker, J.H., *J. Am. Chem. Soc*., 1951, vol. 73, p. 1145.
21. Avdeenko, A.P., Konovalova, S.A., and Ludchenko, O.N., *Russ. J. Org. Chem*., 2006, vol. 42, p. 683.
22. Avdeenko, A.P. and Konovalova, S.A., *Russ. J. Org. Chem*., 2006, vol. 42, p. 669.