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ОРГАНИЧЕСКАЯ И БИООРГАНИЧЕСКАЯ ХИМИЯ

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SYNTHESIS AND ANTIBACTERIAL PROPERTIES OF NEW SULFONAMIDES BASED ON SUBSTITUTED ARYLALKYL-, 1,4-BENZODIOXAN-2-ALKYL-, ISOCHROMAN-1-METHYLAMINES AND 6,7-DIMETHOXY-1-METHYL-1,2,3,4-TETRAHYDROISOQUINOLINE

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The reaction of arylcyclopentyl(tetrahydropyranyl)methyl-, 1,4-benzodioxan-2-yl-methyl (ethyl)-, isochroman-1-methylamines and 6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydro-isoquinoline with phenylsulfo- and tosylchlorides afforded the corresponding substituted sulfonamides. The antibacterial activity of synthesized compounds was investigated.

References 14.

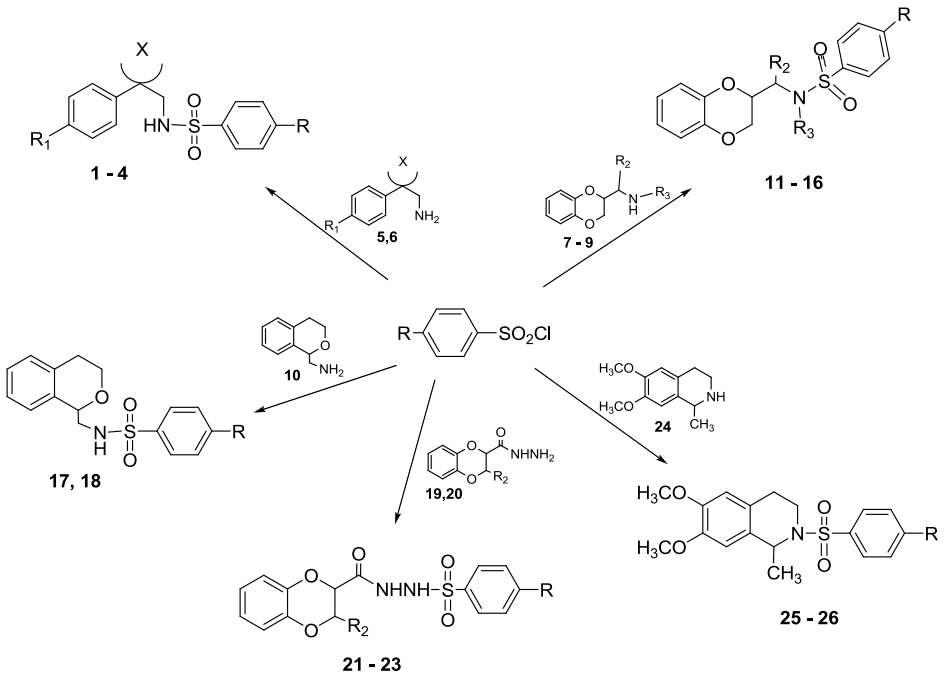
The interest in derivatives of oxygen- and nitrogen-containing heterocycles: 1,4-benzodioxane, isochromane, tetrahydroisoquinoline and opening analogs of the latter is determined by their high and diverse pharmacological activity. With a view to reveal effective biologically active substances in this series, over a number of years we have carried our studies on the synthesis of new amines, amino alcohols, amino amides and diamides possessing adrenolytic, sympatholytic, antiarrhythmic and antihypoxic properties [1].

The compounds with arylsulfonamide fragments are widely used as a highly effective antibacterial medicine for treating various diseases [2].

In the present study the synthesis of new arylsulfonamides is described. As amino components different amines such as phenylcyclopentyl-, 4-methoxyphenylpyranylmethyl, 1,4-benzodioxan-2-ylmethyl-, 1-(1,4-

benzodioxan-2-yl)ethyl, isochroman-1-ylmethylamines and 1-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline are used.

Recent investigations have shown that some compounds with fragments of arylcyclo-pentyl- and aryltetrahydropyranylmethylamines possess diverse biological activities [3, 4]. In continuation of these studies we have synthesized new sulfonamides **1-4** with high yields by condensation of amines **5** and **6** with benzenesulfo- and tosylchlorides in the mixture benzene-water, applying KOH.



X=$(CH_2)_4$, R_1=H: R=H(**1**); R=CH_3(**2**). X=$(CH_2CH_2)_2O$, R_1=CH_3O: R=H(**3**); R=CH_3(**4**). X=$(CH_2)_4$, R_1=H(**5**); X=$(CH_2CH_2)_2O$, R_1=CH_3O(**6**); R_2=R_3=H(**7**); R_2=H, R_3=Et (**8**);R_3=H, R_2=CH_3 (**9**); R=R_2=R_3=H(**11**); R_2=R_3=H, R=CH_3(**12**); R=R_2=H, R_3=Et (**13**); R=CH_3, R_2=H, R_3=Et (**14**); R=R_3=H, R_2=CH_3 (**15**); R=R_2=CH_3, R_3=H (**16**). R=H (**17**), R=CH_3(**18**). R_2=H (**19**); R_2=CH_3 (**20**); R=R_2=H (**21**); R_2=H, R= CH_3(**22**); R=H, R_2=CH_3 (**23**). R=H (**25**), R=CH_3(**26**).

In order to investigate the structure-activity relationship, the sulfonamides with heteryl fragments were obtained. It is known that derivatives of 1,4-benzodioxane and isochromane exhibit high pharmacological activity and are widely used in modern medical practice [5]. For this reason on the basis of heterylalkylamines, in particular 1,4-benzodioxan-2-ylmethylamines (**7,8**), 1-(1,4-benzodioxan-2-yl)ethylamine (**9**) and isochroman-1-ylmethylamine (**10**), the new sulfonamide derivatives **11 -16, 17,18** were synthesized.

When 1,4-benzodioxan-2- and 3-methyl-1,4-benzodioxan-2-carboxylic acid hydrazide (**19,20**) was used as a key starting compound in these syntheses, the sulfonamide derivatives **21 - 23** were obtained. In this case the target compounds were isolated in high yields by treatment of water-alkaline solution with dilute aqueous HCl.

In extension of these investigations and aiming at the search for new bioactive compounds, in the present study we also describe the synthesis of sulfonamides in which a nitrogen atom is included in the heterocyclic ring of the tetrahydroisoquinoline fragment. By interaction of 6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline (**24**) with the above- mentioned sulfochlorides corresponding sulfonamides **25, 26** were synthesized. The structure and purity of the synthesized compounds were confirmed by physicochemical methods and thin-layer chromatography.

The antibacterial activity of compounds was studied by the diffusion method in agar [6] at a bacterial load of 20 *million* microbes per 1 *mL* of medium. Gram- positive staphylococci (Staphylococcus aureus 209 p,1) and gram-negative bacilli (Shegella Flexneri 6858, E. coli 0-55) were used in the experiments. Solutions of test compounds and a control preparation were prepared in DMSO in a dilution of 1:20. Solutions of test substances (0.1 *mL*) were added into Petri dishes containing cultures of the above strains of microorganisms. Diameter (d, *mm*) of microorganisms growth inhibition zone after daily growth of test cultures in a thermostat at 37°C was measured. Furazolidone was used as a positive control [2]. It was found that the test compounds showed low activity, suppressing the growth of all the strains of microorganisms used in the 10-12 *mm* diameter zone significantly inferior to the control drug (d= 24-25 *mm*)

Experimental

The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were measured on a Varian Mercury-300 instrument from solutions in DMSO-d6 using tetramethylsilane as internal reference. The melting points were determined on a Boetius hot stage. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using benzene–acetone (3:1) as eluent; development with iodine vapor.

(1-Phenylcyclopentyl)methanamine (**5**) and **(4-(4-methoxy-phenyl)tetrahydro-2H-pyran-4-yl)methanamine** (**6**) were synthesized according to the procedure reported in [7,8].

(2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)methanamine (**7**), **N-((2,3-dihydrobenzo[b] [1,4]dioxin-2-yl)methyl)ethanamine** (**8**), **1-(2,3-dihydrobenzo[b][1,4] dioxin-2-yl)ethanamine** (**9**) and **isochroman-1-ylmethanamine** (**10**) were prepared as described in [9-12].

2,3-Dihydrobenzo[b][1,4]dioxine-2-carbohydrazide (**19**) and **3-methyl-2,3-dihydrobenzo[b][1,4]dioxine-2-carbohydrazide** (**20**) were synthesized according to the procedure reported in [13, 14].

General procedure for the preparation of Sulfonamides. A solution of 1.7 *g* (30 *mmol*) of KOH in 15 *ml* of water was slowly added to a solution of 15 *mmol* of the amino compounds (**5-10,19, 20, 24**) in 45 *ml* of benzene at 5°C. After cooling the mixture at -2°C, 17 *mmol* in 20 *ml* benzene of the corresponding sulfochloride was slowly added, stirred at this temperature for 5 *h*. The mixture was left overnight and heated for 10-12 *h* at 70-75°C. The organic layer was washed with dilute hydrochloric acid (1: 3), water, a 5% solution of Na_2CO_3 and again water, dried with Na_2SO_4. The solvent was distilled off, the residue was crystallized by ether and recrystallized.

N-((1-Phenylcyclopentyl)methyl)benzenesulfonamide (**1**).Yield 81%, mp 82-84°C (ether), R_f 0.45. IR spectrum, ν, cm^{-1}: 3280(NH), 1607, 1568 (arom.), 1329, 1158 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.56-1.76 m (4H), 1.79-1.89 m (2H) and 1.93-2.03 m (2H, C_5H_8), 2.82 d (2H, J=6.7, NCH_2), 7.02 br. t (1H, J=6.5, NH), 7.11-7.18 m (1H) and 7.20-7.25 m (4H, C_6H_5), 7.48-7.55 m (3H) and 7.68-7.73 m (2H, C_6H_5S). ^{13}C NMR spectrum, δ_C, ppm: 22.9, 34.8, 50.8, 51.2, 125.1, 126.3, 126.5, 127.4, 128.1, 131.0, 140.9, 146.1. Found, %: C 68.87; H 6.89; N 4.71. $C_{18}H_{21}NO_2S$. Calculated, %: C 68.54; H 6.71; N 4.44.

4-Methyl-N-((1-phenylcyclopentyl)methyl)benzenesulfonamide (**2**).Yield 78%, mp 98-100°C (benzene), R_f 0.48. IR spectrum, ν, cm^{-1}: 3271(NH), 1609, 1578 (arom.), 1331, 1164 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.56-1.76 m(4H), 1.78-1.88 m (2H) and 1.92-2.02 m(2H, C_5H_8), 2.41 s (3H, CH_3), 2.80 d (2H, J=6.7, NCH_2), 6.92 br. T (1H, J=6.7, NH), 7.09-7.16 m (1H, C_6H_5), 7.20 -7.25 m (6H, Ar), 7.56-7.60 m (2H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 20.8, 22.9, 34.8, 50.8, 51.2, 125.1, 126.3, 126.5, 127.4, 128.7, 138.0, 141.2, 146.2. Found, %: C 69.41; H 7.32; N 4.53. $C_{19}H_{23}NO_2S$. Calculated, %: C 69.27; H 7.04; N 4.25.

N-((4-(4-Methoxyphenyl)tetrahydro-2H-pyran-4-yl)methyl)benzene-sulfonamide (3). Yield 76%, mp 142-144°C (ethanol), R_f 0.51. IR spectrum, ν, cm^{-1}: 3269(NH), 1610, 1573 (arom.), 1337, 1172 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.85 ddd (2H, J=14.0, 9.4, 3.9, CH_2), 1.93-2.02 m (2H, CH_2), 2.78 d (2H, J=6.6, NCH_2), 3.38 ddd (2H, J=11.4, 9.4, 2.6, OCH_2), 3.64 ddd (2H, J= 11.4, 5.0, 3.5, OCH_2), 3.77 s (3H, OCH_3), 6.78-6.83 m (2H, C_6H_4), 7.12 br.t (1H, J=6.6, NH) 7.13-7.18 m (2H, C_6H_4), 7.41-7.54 m (3H, meta, para- C_6H_5), 7.68-7.73 m (2H, orto-C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 32.7, 39.1, 53.1, 54.4, 62.9, 113.3, 126.2, 127.6, 128.1, 131.1, 134.3, 140.9, 157.2. Found, %: C 63.39; H 6.72; N 4.12. $C_{19}H_{23}NO_4S$. Calculated, %: C 63.13; H 6.41; N 3.88.

N-((4-(4-Methoxyphenyl)tetrahydro-2H-pyran-4-yl)methyl)-4-methylbenzenesulfonamide (4). Yield 79%, mp 160-162°C (ethanol), R_f 0.53.

IR spectrum, ν, cm^{-1}: 3284(NH), 1608, 1570 (arom.), 1340, 1155 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.84 ddd (2H, J=14.0, 9.4, 3.9, CH_2), 1.93-2.02 m (2H, CH_2), 2.40 s (3H, CH_3), 2.81 d (2H, J=6.6, NCH_2), 3.37 ddd (2H, J=11.3, 9.4, 2.6, OCH_2), 3.64 ddd (2H, J= 11.3, 5.0, 3.5, OCH_2), 3.78 s (3H, OCH_3), 6.78-6.83 m (2H) and 7.13-7.18 m (2H, C_6H_4O), 7.13 br.t (1H, J=6.6, NH), 7.27-7.34 m (2H) and 7.66-7.73 m (2H, C_6H_4). Found, %: C 64.20; H 6.93; N 4.06. $C_{20}H_{25}NO_4S$. Calculated, %: C 63.97; H 6.71; N 3.73.

N-((2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)methyl)benzenesulfonamide (11). Yield 74%, mp 103-104 °C (benzene), R_f 0.54. IR spectrum, ν, cm^{-1}: 3277(NH), 1590, 1500 (arom.), 1314, 1155 (SO_2). ^{1}H NMR spectrum, δ, ppm: 2.92-3.09 m (2H, NCH_2), 3.92 dd (1H, J=11.4, 6.9, OCH_2), 4.12-4.18 m (1H, OCH), 4.28 dd (1H, J= 11.4, 2.3, OCH_2), 6.68-6.79 m (4H, C_6H_4), 7.55-7.67 m (3H) and 7.80-7.84 m (2H, C_6H_5), 7.77 br.t (1H, J=5.8, NH). Found, %: C 59.31; H 5.21; N 4.86. $C_{15}H_{15}NO_4S$. Calculated, %: C 59.00; H 4.95; N 4.59.

N-((2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)methyl)-4-methylbenzenesulfonamide (12). Yield 72%, mp 110-112°C (ethanol), R_f 0.52. IR spectrum, ν, cm^{-1}: 3274(NH), 1591, 1497 (arom.), 1335, 1159(SO_2). ^{1}H NMR spectrum, δ, ppm: 2.43 s (3H, CH_3), 2.93-3.10 m (2H, NCH_2), 3.93 dd (1H, J=11.4, 6.9, OCH_2), 4.12-4.19 m (1H, OCH), 4.27 dd (1H, J= 11.4, 2.3, OCH_2), 6.68-6.79 m (4H, C_6H_4), 7.29-7.33 m (2H, $C_6H_4CH_3$),7.68-7.72 m (2H, $C_6H_4CH_3$), 7.78 br.t (1H, J=5.8, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.8, 42.2, 64.9, 71.2, 116.4, 116.6, 120.5, 120.7, 126.4, 128.9, 137.6, 141.7, 142.3, 142.6. Found, %: C 60.39; H 5.64; N 4.61. $C_{16}H_{17}NO_4S$. Calculated, %: C 60.17; H 5.37; N 4.39.

N-((2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)methyl)-N-ethylbenzenesulfonamide (13). Yield 72%, mp 64-65°C (benzene), R_f 0.46. IR spectrum, ν, cm^{-1}: 1590, 1494 (arom.), 1333, 1161 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.13 t (3H, J=7.1, CH_3), 3.17-3.38 m (2H, $NC\mathbf{H_2}CH_3$), 3.45 dd (1H, J=15.0, 5.2, NCH_2), 3.34 dd (1H, J=15.0, 6.2, NCH_2), 4.03 dd (1H, J= 11.4, 6.6, OCH_2), 4.33 dd (1H, J= 11.4, 2.3, OCH_2), 4.35-4.42 m (1H, OCH), 6.71-6.81 m (4H, C_6H_4), 7.53-7.65 m (3H, C_6H_5), 7.81-7.85 m (2H, C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 13.3, 44.1, 47.5, 65.0, 71.7, 116.5, 116.6, 120.7, 120.8, 126.6, 128.6, 132.0, 139.1, 142.0, 142.6. Found, %: C 61.47; H 6.00; N 4.48. $C_{17}H_{19}NO_4S$. Calculated, %: C 61.24; H 5.74; N 4.20.

N-((2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)methyl)-N-ethyl-4-methylbenzenesulfonamide (14). Yield 74%, mp 76-78°C (benzene), R_f 0.50. IR spectrum, ν, cm^{-1}: 1595, 1490 (arom.), 1336, 1165 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.14 t (3H, J=7.1, $CH_2C\mathbf{H_3}$), 2.41 s (3H, CH_3), 3.18-3.39 m (2H, $C\mathbf{H_2}CH_3$), 3.34 dd (1H, J=15.0, 6.2, NCH_2), 3.46 dd (1H, J=15.0, 5.2, NCH_2), 4.03 dd (1H, J= 11.4, 6.6, OCH_2), 4.33 dd (1H, J= 11.4, 2.3, OCH_2), 4.38-4.45 m (1H, OCH), 6.70-6.80 m (4H, C_6H_4), 7.30-7.35 m (2H) and

7.70-7.75 m (2H, C_6H_4S). Found, %: C 62.52; H 6.31; N 4.29. $C_{18}H_{21}NO_4S$. Calculated, %: C 62.23; H 6.09; N 4.03.

N-(1-(2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)ethyl)benzenesulfonamide (15). Yield 67%, mp 134-135°C (ethanol), R_f 0.46. IR spectrum, ν, cm^{-1}: 3275(NH), 1596, 1500 (arom.), 1332, 1159(SO_2). Two diastereomers, 1/1. ^{1}H NMR spectrum, δ, ppm: 1.02d (1.5H, J=6.8, C**H$_3$**CH), 1.05d (1.5H, J=6.8, C**H$_3$**CH), 3.40-3.45 m (0.5H) and 3.52 -3.57 m (0.5H, C**H**CH_3), 3.81 - 4.00 m (2H) and 4.23-4.37 m (1H, OCH_2CHO), 6.70-6.78 m (4H, C_6H_4), 7.45-7.60 m (3H) and 7.78-7.88 m (3H, NH and C_6H_5). Found, %: C 60.36; H 5.59; N 4.62. $C_{16}H_{17}NO_4S$. Calculated, %: C 60.17; H 5.37; N 4.39.

N-(1-(2,3-Dihydrobenzo[b][1,4]dioxin-2-yl)ethyl)-4-methylbenzene-sulfonamide (16). Yield 64%, mp 120-121°C (toluene), R_f 0.51. IR spectrum, ν, cm^{-1}: 3270(NH), 1598, 1498 (arom.), 1338, 1162 (SO_2). Two diastereomers, 1/1. ^{1}H NMR spectrum, δ, ppm: 1.01d (1.5H, J=6.8, C**H$_3$**CH), 1.04d (1.5H, J=6.8, C**H$_3$**CH), 2.44 s (3H, CH_3Ar), 3.25-3.37 m (0.5H) and 3.42-3.53 m (0.5H, C**H**CH_3), 3.77-4.00 m(2H) and 4.22-4.36 m (1H, OCH_2CHO), 6.66-6.78 m (4H, C_6H_4), 7.27-7.34 m (2H, C_6**H$_4$**CH_3), 7.66-7.75 m (3H, NH and C_6**H$_4$**CH_3). ^{13}C NMR spectrum, δ_C, ppm: 15.8 and 16.5, 20.8, 48.7 and 48.8 , 64.7 and 64.8, 74.6 and 75.0, 116.3, 116.4, 116.4 and 116.5, 120.4, 120.5, 120.5 and 120.5, 126.3 and 126.3, 128.8 and 128.9, 138.7 and 138.9, 141.5 and 141.6, 142.4 and 142.8, 142.8 and 143.0. Found, %: C 61.53; H 5.92; N 4.58. $C_{17}H_{19}NO_4S$. Calculated, %: C 61.24; H 5.74; N 4.20.

N-(Isochroman-1-ylmethyl)benzenesulfonamide (**17**).Yield 80%, mp 85-86°C (ethanol), R_f 0.47. IR spectrum, ν, cm^{-1}: 3242 (NH), 1331, 1167 (SO_2). ^{1}H NMR spectrum, δ, ppm: 2.69 ddd (1H, J=16.2, 5.1, 4.4, CH_2), 2.82 ddd (1H, J=16.2, 7.8, 5.0, CH_2), 3.06 ddd (1H, J=13.5, 8.5, 4.8, NCH_2), 3.23 ddd (1H, J=13.5, 6.1, 3.2, NCH_2), 3.66 ddd (1H, J=11.4, 7.8, 4.3, OCH_2), 3.96 ddd (1H, J=11.4, 5.1, 5.1, OCH_2), 4.70 dd (1H, J=8.5, 3.2, CH), 7.01-7.13 m (4H, C_6H_4), 7.47-7.57 m (4H, NH and meta, para-C_6H_5), 7.81-7.86 m (2H, orto-C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 28.1, 46.8, 61.1, 73.9, 124.5, 125.5, 126.0, 126.3, 128.2, 128.2, 131.2, 133.4, 134.5, 141.0. Found, %: C 63.61; H 5.88; N 4.93. $C_{16}H_{17}NO_3S$. Calculated, %: C 63.34; H 5.65; N 4.62.

N-(Isochroman-1-ylmethyl)-4-methylbenzenesulfonamide (**18**).Yield 82%, mp 96-97°C (benzene), R_f 0.52. IR spectrum, ν, cm^{-1}: 3244(NH), 1329, 1165 (SO_2). ^{1}H NMR spectrum, δ, ppm: 2.42 s (3H, CH_3), 2.70 ddd (1H, J=16.2, 5.1, 4.4, CH_2), 2.84 ddd (1H, J=16.2, 7.8, 5.0, CH_2), 3.07 ddd (1H, J=13.5, 8.5, 4.8, NCH_2), 3.24 ddd (1H, J=13.5, 6.1, 3.2, NCH_2), 3.66 ddd (1H, J=11.4, 7.8, 4.3, OCH_2), 3.97 ddd (1H, J=11.4, 5.1, 5.1, OCH_2), 4.71 dd (1H, J=8.5, 3.2, CH), 7.02-7.13 m (4H, C_6H_4), 7.30-7.35 m (2H) and 7.70-7.75 m (2H, C_6H_4S), 7.78 br.t (1H, J=5.8, NH). Found, %: C 64.58; H 5.98; N 4.62. $C_{17}H_{19}NO_3S$. Calculated, %: C 64.33; H 6.03; N 4.41

N`-(2,3-Dihydrobenzo[b][1,4]dioxine-2-carbonyl)benzenesulfonohydrazide (21). Yield 76%, mp 210-212°C (ethanol), R_f 0.36. IR spectrum, ν, *cm*$^{-1}$: 3320, 3067 (NH), 1682 (C=O), 1347, 1163 (SO_2). ^{1}H NMR spectrum, δ, ppm: 4.01 dd (1H, J=11.4, 6.1, CH_2), 4.13 dd (1H, J=11.4, 2.8, CH_2), 4.61 dd (1H, J=6.1,2.8, CH), 6.76-6.84 m (3H) and 6.86-6.91 m (1H, C_6H_4), 7.43-7.49 m (2H, meta - C_6H_5), 7.53-7.59 m (1H, para-C_6H_5), 7.74-7.79 m (2H, orto-C_6H_5), 9.90 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 64.3, 71.3, 116.6, 117.0, 120.9, 121.0, 127.6, 128.1, 132.1, 138.7, 141.9, 142.6, 165.0. Found, %: C 54.12; H 4.51; N 8.60. $C_{15}H_{14}N_2O_5S$. Calculated, %: C 53.88; H 4.22; N 8.38.

N`-(2,3-Dihydrobenzo[b][1,4]dioxine-2-carbonyl)-4-methylbenzenesulfonohydrazide (22). Yield 73%, mp 188-190°C (ethanol), R_f 0.42. IR spectrum, ν, *cm*$^{-1}$: 3324, 3073 (NH), 1680 (C=O), 1341, 1160 (SO_2). ^{1}H NMR spectrum, δ, ppm: 2.43 s (3H, CH_3), 4.03 dd (1H, J=11.4, 6.1, CH_2), 4.15 dd (1H, J=11.4, 2.8, CH_2), 4.64 dd (1H, J=6.1, 2.8, CH), 6.78-6.90 m (4H, C_6H_4), 7.43-7.49 m (2H) and 7.55-7.60 m (2H, C_6H_4S), 9.91 br.s (2H, NH). Found, %: C 55.38; H 4.83; N 8.37. $C_{16}H_{16}N_2O_5S$. Calculated, %: C 55.16; H 4.63; N 8.04.

N`-(3-Methyl-2,3-dihydrobenzo[b][1,4]dioxine-2-carbonyl)benzenesulfonohydrazide (23). Yield 75%, mp 208-209°C (ethanol), R_f 0.38. IR spectrum, ν, *cm*$^{-1}$: 3317, 3052 (NH), 1679 (C=O), 1340, 1159 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.16 d (3H, CH_3, J=6.3Hz), 4.02 dk(1H, C**H**CH_3, J= 6.8,6.3 Hz), 4.12 d (1H, CHCO, J= 6.8 Hz), 6.73-6.81 m(3H) and 6.82-6.89 m(1H, C_6H_4), 7.46-7.53 m (2H, m-C_6H_5), 7.56-7.62 m (1H, p-C_6H_5), 7.82 - 7.87 m (2H, o-C_6H_5), 9.80 br.s (1H, NH), 10.48b.s (1H, NH). Found, %: C 55.29; H 4.79; N 8.30. $C_{16}H_{16}N_2O_5S$. Calculated, %: C 55.16; H 4.63; N 8.04.

6,7-Dimethoxy-1-methyl-2-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (25). Yield 74%, mp 90-92°C (toluene), R_f 0.41. IR spectrum, ν, *cm*$^{-1}$: 1600, 1490 (arom.), 1372, 1160 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.40 d (3H, J=6.7, CH_3), 2.46-2.63 m (2H, CH_2), 3.35 ddd (1H, J=13.7, 9.9, 6.0, NCH_2), 3.70 s (3H, OCH_3), 3.75 s (3H, OCH_3), 3.82 ddd (1H,J=13.7, 5.5, 3.0, NCH_2), 5.00 k (1H, J=6.7, CH), 6.42 s(1H,C_6H_2), 6.60 s (1H, C_6H_2), 7.42-7.55 m (3H, meta, para-C_6H_5), 7.73-7.77 m (2H, orto-C_6H_5). Found, %: C 62.47; H 6.39; N 4.29. $C_{18}H_{21}NO_4S$. Calculated, %: C 62.23; H 6.09; N 4.03.

6,7-Dimethoxy-1-methyl-2-tosyl-1,2,3,4-tetrahydroisoquinoline (**26**).Yield 77%, mp 157-159°C (ethanol), R_f 0.46. IR spectrum, ν, *cm*$^{-1}$: 1610, 1500 (arom.), 1338, 1170 (SO_2). ^{1}H NMR spectrum, δ, ppm: 1.39 d (3H, J=6.7, C**H**$_3$CH), 2.39 s (3H, CH_3), 2.46-2.64 m (2H, CH_2), 3.32 ddd (1H, J=13.7, 10.3, 5.5, NCH_2), 3.71 s (3H, OCH_3), 3.75 s (3H, OCH_3), 3.74 - 3.82 m (1H, NCH_2), 4.96 k (1H, J=6.7, CH), 6.43 s (1H, C_6H_2), 6.59 s (1H,

C_6H_2), 7.22-7.27 m (2H, C_6H_4), 7.59-7.64 m (2H, C_6H_4). Found, %: C 63.38; H 6.70; N 4.09. $C_{19}H_{23}NO_4S$. Calculated, %: C 63.13; H 6.41; N 3.88.

ՏԵՂԱԿԱԼՎԱԾ ԱՐԻԼԱԼԿԻԼ-, 1,4-ԲԵՆԶՈԴԻՕՔՍԱՆ-2-ԱԼԿԻԼ-, ԻԶՈՔՐՈՄԱՆ-1-ՄԵԹԻԼԱՄԻՆՆԵՐԻ ԵՎ 6,7-ԴԻՄԵԹՕՔՍԻ-1-ՄԵԹԻԼ-1,2,3,4-ՏԵՏՐԱՀԻԴՐՈԻԶՈՔԻՆՈԼԻՆԻ ՀԻՄԱՆ ՎՐԱ ՆՈՐ ՍՈՒԼՖՈՆԱՄԻԴՆԵՐԻ ՍԻՆԹԵԶՆ ՈՒ ՀԱԿԱԲԱԿՏԵՐԻԱԼ ՀԱՏԿՈՒԹՅՈՒՆՆԵՐԸ

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Տեղակալված սուլֆոնամիդների շարքում կառուցվածք-կենսաբանական ակտիվություն կապի որոշակի օրինաչափություններ բացահայտելու համար սինթեզվել են նոր միացություններ տեղակալված արիլալկիլ- և հետերիլ ֆրագմենտներով: Փոխազդեցության մեջ են դրվել բենզոլսուլֆոքլորիդը և տոզիլքլորիդը արիլցիկլոպենտիլ-/կամ տետրահիդրոպիրանիլ/մեթիլամինների, 1,4-բենզոդիօքսան-2-մեթիլ/կամ էթիլ/-, իզոքրոման-1-մեթիլամինների, ինչպես նաև 6,7-դիմեթօքսի-1-մեթիլ-1,2,3,4-տետրահիդրոիզոքինոլինի հետ, որի արդյունքում ստացվել են նպատակային սուլֆոնամիդներ: Ուսումնասիրվել են սինթեզված միացությունների հակաբակտերիալ հատկությունները:

СИНТЕЗ И АНТИБАКТЕРИАЛЬНЫЕ СВОЙСТВА НОВЫХ СУЛЬФОНАМИДОВ НА ОСНОВЕ ЗАМЕЩЕННЫХ АРИЛАЛКИЛ-, 1,4- БЕНЗОДИОКСАН-2-АЛКИЛ-, ИЗОХРОМАН-1-МЕТИЛАМИНОВ И 6,7-ДИМЕТОКСИ-1-МЕТИЛ-1,2,3,4-ТЕТРАГИДРОИЗОХИНОЛИНА

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С целью выявления определенных закономерностей связи “структура–биологическая активность” в ряду замещенных сульфонамидов нами предпринят синтез новых соединений, содержащих арилалкильные и гетерильные фрагменты. Для этого взаимодействием бензолсульфохлорида и тозилхлорида с арилциклопентил (или тетрагидропиранил)метиламинами и (1,4-бензодиоксан-2-ил)-метил(или этил)-, изохроман-1-метиламинами, а также с 6,7-диметокси-1-метил-1,2,3,4-тетрагидроизохинолином синтезированы соответствующие целевые вещества. Изучены антибактериальные свойства полученных соединений.

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