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SYNTHESIS OF NEW DERIVATIVES OF 2-R-6R'-4-QUINOLINE CARBOXYLIC ACIDS FROM A SERIES OF HETARYL QUINOLINES

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As a result of intramolecular heterocyclization of thiosemicarbazides of 2-substituted quinoline-4-carboxylic acids in alkaline and acidic media, new derivatives of 2-substituted quinoline-4-carboxylic acids containing triazole and thiadiazole rings, compounds from the series of hetarylquinolines, were isolated. Acylation of the corresponding 1,3,4-thiadiazol-2-amines gave 1,3,4-thiadiazol-2-yl-acetamides-2, 6-substituted-4-quinolinecarboxylic acids. All synthesized compounds are potentially biologically active compounds, and further study of their activity is promising.

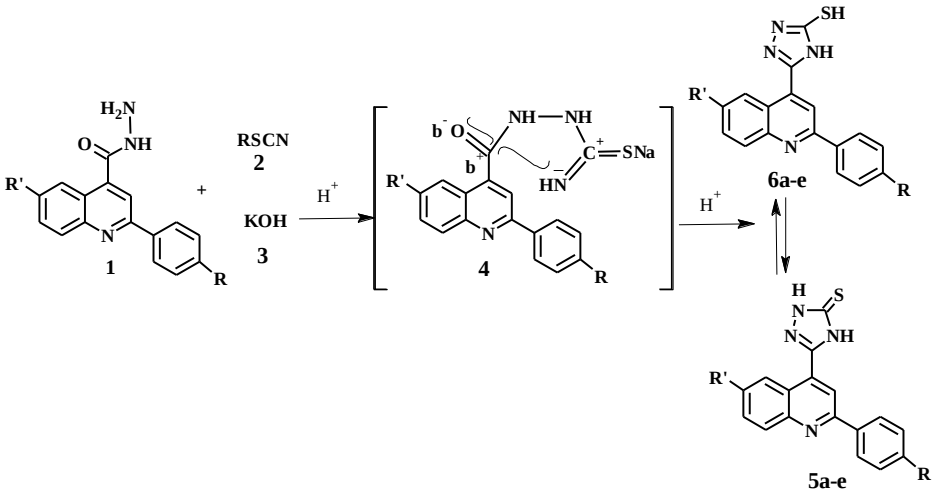
References 18.

At present, a fairly large number of natural and synthetic derivatives of 2-substituted-4-quinolinecarboxylic acids with pronounced biological activity are known [1-4]. On the other hand, from literature data it is known that derivatives of 1,3,4-thiadiazoles have a different spectrum of biological activity. Among the representatives of a number of thiadiazoles there are compounds exhibiting antimicrobial, antifungal, antiviral, antitumor, herbicidal and insecticidal activities [5,6]. Based on compounds containing a 1,3,4-thiadiazole fragment, preparations have been developed that are widely used in medical practice: diacarb is a diuretic from the group of carbonic anhydrase inhibitors, etazole is a sulfanilamide preparation [7-10]. The presence of diverse biological activities in the rows of 1,2,4-triazoles and 1,3,4-thiadiazoles [11-14] prompted us to consider ways of combining these two fragments in one molecule and to study the antibacterial activity of the compounds obtained.

We synthesized 1,2,4-triazoles by three-component condensation of hydrazides **1**, potassium thiocyanate **2,** concentrated hydrochloric acid, followed by the addition of sodium hydroxide **3.** The starting acids **1-3** were

obtained from methylketones and isatines by the Pfitzinger reaction [15]. Hydrazides **1** were obtained by heating compounds in excess of hydrazine hydrate in ethyl alcohol, according to the method [16]. After purification, hydrazides were obtained in of 74-76% yields. The IR spectra contain cm^{-1} absorption bands, respectively. As can be seen from the Scheme, under the action of alkali, the thiosemicarbazides **4a-e** are completely converted to thiolates, then due to the attack of the nucleophilic nitrogen atom of the electron-deficient carbon atom of the carbonyl group, the heterocyclic system **5a-e** is formed. As a result of the cyclization process, the formation of two isomeric products -2-substituted-4-quinoline-1,2,4-triazole-5-thiones **5a-e** and 2-substituted-4-quinoline-5-mercapto-1,2,4-triazoles **6a-e** is possible according to Scheme 1.

Scheme 1



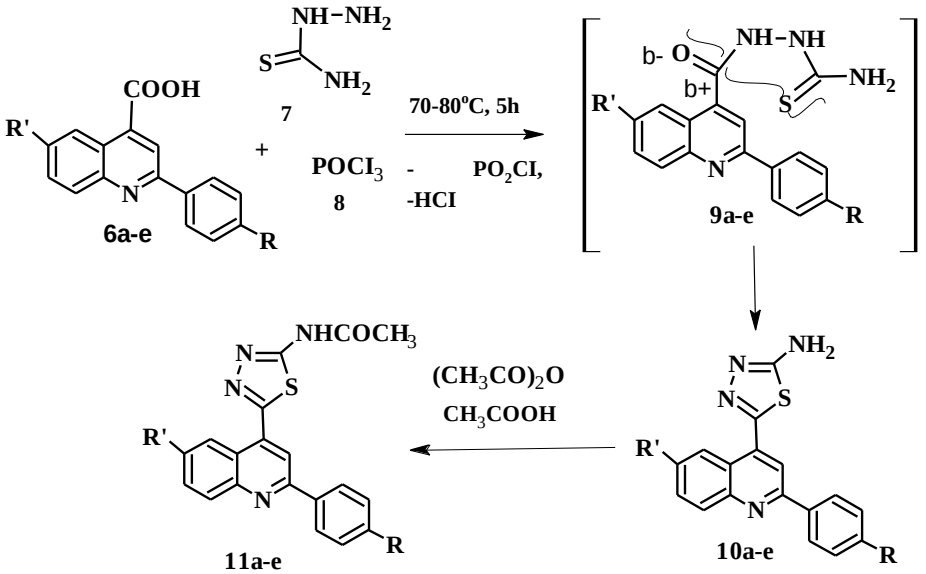
R^1=H: R= Ph, (**5a**); R=C_6H_4CI-4(**5b**); R=C_6H_4Br-4(**5c**); R=C_6H_4-OCH_3 (**5d**); R^1=Br: R=C_6H_4-OCH_3 (**5e**).

To find out which structure to give preference to, we studied the absorption spectrum in the infrared region of reaction products **5a-e.** The IR spectrum of compounds **5a-e** contains two deformation absorption maxima at 1380–1382 cm^{-1}, characteristic for vibrations of the > C = S group of 1,2,4-triazole-5-thione, and stretching vibrations of the > CSH bonds in the 2500 region -2475 are either very weak or absent. Thus, during the reaction product processing, an isomer containing mainly a thionic group > C = S is released. However, this group is labile and capable of easily rearranging to the sulfhydryl group > C-S-H. In the NMR spectrum of 1,2,4-triazole-5-thiol **5a-e** in deuterated chloroform, the proton signals and their integral curves exactly correspond to the structure of the compound. Thus, in the NMR spectra of compounds **5a-e**, broadened singlet signals with an intensity of 2 protons of the NH and SH groups are observed at 11.35 ppm, a group of signals characteristic of the quinoline ring is manifested in the region of 7.60, 7.74, 8.12, 8.45, 8.46 *ppm* with a total

intensity of 5 protons and chemical shifts of the phenyl ring are manifested in 7.42-7.55, 8.23-8.28 ppm with a total intensity of 5 protons.

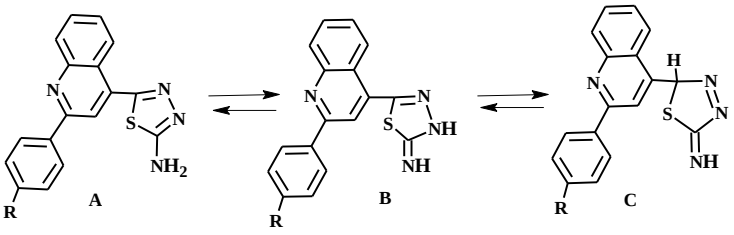
The synthesis of 5-[2-(4-substituted phenyl)quinolin-4-yl]-1,3,4-thiadiazol-2-amines **10a-e** was carried out by the known method for the cyclization of respectively substituted thiosemicarbazides. By reaction with $POCI_3$, the corresponding acids are converted into acid chlorides and then the nucleophilic addition of thiosemicarbazide to the carbonyl group and subsequent proton migration lead to the intermediate, which is the thiosemicarbazide acid. Under the influence of an acidic medium, the latter undergoes intramolecular heterocyclization due to the attack of the sulfur nucleophilic center by the electron-deficient carbon atom with the formation of target compounds **10a-e** in 42% yield, according to Scheme 2.

Scheme 2



1,3,4-Thiadiazole-5-amines **10a-e** can exist in several tautomeric forms, according to Scheme 3.

Scheme 3



The presence in the IR spectrum of compounds **10a-e** of intense absorption in the region of 1699, 1639, 1642, 1627 cm^{-1} [Sharba et. al 2005; Prech et al. 2006; Nakhmanovich et al. 1990], characteristic of vibrations of the 1,3,4-thiadiazole cycle, the presence of absorption in the region of 2503-2485 (characteristic of stretching vibrations of the SH bond in the 1,3,4-

thiadiazole group) and absorption in the region of 3080, 3100 3426 cm^{-1} characteristic of NH_2 groups support structure A. The acylation of compounds **10a-e** with acetic anhydride leads to new compounds N1-[5-(2-substituted phenyl-6 substituted-4-quinolyl)-1,3,4-thiadiazol-2-yl] acetamides **11a-e** (Scheme 2) [16]. In the ^{13}C NMR spectrum of compounds **11a-e**, two signals were detected in the region with a chemical shift of 149.3 and 159.3 ppm characteristic of carbon atoms in the 1,3,4-thiadiazole core. Compounds **11a–e** had a characteristic absorption band of about 1668-1667 cm^{-1} for the NHC = O group; and one proton signal of the CH_3 group in the δ 2.06-2.16 ppm range.

The antibacterial activities of compounds **5a-e, 10a-e, 11a–e** were studied according to the procedure [17] with a bacterial load of 20 million microbial bodies per 1 *ml* of medium. Gram-positive staphylococci (Staphylococcus aureus 209p, 1) and gram-negative bacilli (Sh. Fleaneri 6858, E.coli 0-55) were used in the experiments. Compounds were tested at a 1:20 dilution prepared in DMSO. On Petri dishes with crops of the above strains of microorganisms, solutions of the tested substances in a volume of 0.1 ml were applied. The results were taken into account according to the diameter (d, mm) of the zones of the absence of microorganism growth at the place of application of the substances after daily 489 cultivation of test cultures in a thermostat at 37°C. The known drug furazolidone was used as a positive control [18]. It was found that **5a-e, 10 a-e** exhibited weak antimicrobial activity against all strains used (d = 10-14 *mm*), while the activity of the N-acylation products **11a-e** increased significantly (d = 16-22 *mm*), however, it was slightly inferior to the control drug furazolidone (d = 24-25 *mm*).

The synthesized compounds **5a-e, 10a-e**, and **11a-e** from a number of hetaryl quinolines are the starting compounds for the synthesis of new potentially biologically active substances.

Experimental part

IR spectra were recorded on a “Nicolet Avatar 330 FT-IR” spectrometer. ^1H NMR spectra were recorded on a “Mercury 300-VX” spectrometer with a resonant frequency of 300.08 *MHz*, in a DMSO + CF_3COOD solution; internal standard – TMS. Melting points of the obtained substances were determined on a Boetius instrument. The individuality of substances was monitored by TLC on “Silufol-254” plates in the system butanol – ethanol – acetic acid – water (8:2:1:3), and the developer was iodine pairs.

Synthesis of 5-(2-substituted phenyl-4-quinolyl)-3H-1,2,4-triazole-3-thiones (5a-e). (General methodology). A solution of hydrazide (3.57 *mmol*), potassium thiocyanate 1g (10.71 *mmol*), concentrated hydrochloric acid 4 *ml* and 50 *ml* water is stirred at room temperature for 24 hours. Sodium hydroxide 4% (60 *ml*) is added to the resulting suspension and stirred for 24 hours at 60-70°C. The resulting mixture is neutralized with

hydrochloric acid and the resulting precipitate is filtered, washed with acetone and purified twice by crystallization in ethanol.

5-(2-Phenylquinolin-4yl)-2,4-dihydro-3H-1,2,4-triazole-3-thion (5a). Yield 71%, mp 220-222°C, Rf 0.64. IR spectrum, υ, *cm*$^{-1}$: 3445 (NH); 3113 (C-H), 1380 (C = S). ^{1}H NMR, spectrum, d, ppm: 7.42-7.55 m (3H, C_6H_5); 7.60 ddd, (1H, J = 8.5, 6.9, 1.3, C_6H_4); 7.74 ddd, (1H, J = 8.5, 6.9, 1.3, C_6H_4); 8.12 dd (1H, J = 8.5, 1.3, C_6H_4); 8.23-8.28 m (2H, C_6H_5); 8.45 s (1H, = CH quin); 8.82 (1H, dd, J 8.5, 1.3, C_6H_4); 11.35 s (2H, NH and SH). ^{13}C: 120.8 (CH), 126.1 (CH); 126.1 (CH); 126.5 (CH); 129 (CH); 129.6 and 129.6 (CH, C_6H_4-p); 131.4 (CH); 133.4 (CH); 135.7 (CH); 128.4 (C); 140.1 (C); 146.7 (C); 156.8 (C); 147.8 and 168.3 (C^{17} and C^{16} triazole). Found, %: C 67.05; H 3.94; N, 18.40; S 10.50. $C_{17}H_{12}N_4S$. Calculated, %: C 67.08; H 3.97; N 18.41; S 10.53.

5-[2-(4-Chlorophenyl)quinolin-4yl]-2,4-dihydro-3H-1,2,4-triazole-3-thion(5b). Yield 69%, mp 251-252°C. Rf 0.63. IR spectrum, υ, *cm*$^{-1}$: 3443 (NH); 3113 (C-H), 1382 (C = S). ^{1}H NMR, spectrum, d, ppm: 7.41-7.53 m (3H, C_6H_4CI); 7.58 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 7.73 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 8.10 dd (1H, J = 8.5, 1.3, C_6H_4); 8.22-8.27 m (1H, C_6H_4CI); 8.45 s (1H, = CH quin); 8.81 dd (1H, J = 8.5, 1.3, C_6H_4); 11.35 s (2H, NH and SH). ^{13}C: 120.8 (CH), 126.5 (CH); 129.1 (CH); 129.1 (CH); 130.8 and 130.8 (CH, C_6H_4-p); 131.4 (CH); 133.4 (CH); 135.7 (CH); 128.4 (C); 133.4 (C); 138.9 (C); 140.1. (C); 146.7 (C); 156.9 (C); 147.8 and 168.3 (C^{17} and C^{16} triazole). Found, %: C 60.25; H 3.24; N16.51; S 9.42. $C_{17}H_{11}CIN_4S$. Calculated, %: C 60.26; H 3.27; Cl 10.46; N 16.54; S 9.46.

5-[2-(4-Bromophenyl)quinolin-4-yl]-2,4-dihydro-3H-1,2,4-triazol-3-thion (5c). Yield 61%, mp 280-282°C, Rf 0.61. IR spectrum, υ, *cm*$^{-1}$: 3441 (NH); 3114 (C-H), 1381 (C = S). ^{1}H NMR, spectrum, d, ppm: 7.41-7.53 m (3H, C_6H_4Br); 7.58 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 7.73 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 8.10 dd (1H, J = 8.5, 1.3, C_6H_4); 8.22-8.27 m (1H, C_6H_4Br); 8.45 s (1H, = CH quin); 8.81 dd (1H, J = 8.5, 1.3, C_6H_4); 11.35 s (2H, NH and SH). ^{13}C: 120.3 (CH); 126.5 (CH); 129.4 (CH); 129.4 (CH); 131.3 and 131.3 (CH, C_6H_4-p); 131.4 (CH); 133.4 (CH); 135.7 (CH); 122.9 (C); 130.5 (C); 133.4 (C); 139.3 (C); 140.2 (C); 145.2 (C); 158.6 (C); 147.8 and 168.3 (C^{17} and C^{16} triazole). Found, %: C 60.25; H 3.24; N16.51; S 9.42. $C_{17}H_{11}BrN_4S$. Calculated, %: C 53.27; H 2.89; Br 20.85; N 14.62; S 8.37.

5-[2-(4-methoxyphenyl)quinolin-4-yl]-2,4-dihydro-3H-1,2,4-triazol-3-thion (5e). Yield 61.34%, mp 248-250°C, Rf 0.59. IR spectrum, υ, *cm*$^{-1}$: 3439 (NH); 3114 (C-H), 1380 (C = S). ^{1}H NMR, spectrum, d, ppm: 3.88 s (3H, OCH_3); 6.99-7.04m (2H, C_6H_4); 7.79 dd (1H, = CH, J1 8.9, J2 2.3 Hz, C_6H_4); 7.99 d (1H, = CH, J 8.9 Hz, C_6H_4); 7.58 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 7.73 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 8.10 dd (1H, J = 8.5, 1.3, C_6H_4); 8.46 s (1H, = CH quin); 8.82 dd (1H, J 8.5, 1.3, C_6H_4); 11.30 s (2H, NH and SH). 13 C: 55.3 (^{18}CH3); 114.9 (CH); 114.9 (CH); 120.6 (CH); 126.5 (CH); 129.7 (CH); 129.7 (CH); 131.4 (CH); 133.4 (CH); 135.7 (CH);

128.4 (C); 136. 9 (C); 140.1 (C); 146, 7 (C); 157.3 (C); 159.1 (C); 147.8 and 168.3 (C^{17} and C^{16} triazole.) Found, %: C 52.30; H 3.15; Br 19.31; N 13.54; S 7.73. $C_{18}H_{14}N_4OS$. Calculated, %: C 64.65; H 4.22; N 16.75; S 9.59.

5-[6-Bromo-2-(4-methoxyphenyl)quinolin-4-yl]-2,4-dihydro-3H-1,2,4-triazol-3-one (5e). Yield 51%, mp 250-252°C, Rf 0.64. IR spectrum, υ, cm^{-1}: 3445 (NH); 3114 (C-H), 1380 (C = S). ^{1}H NMR, spectrum, d, ppm: 3.88 s (3H, OCH_3); 6.99-7.04m (2H, C_6H_4); 7.79 dd (1H, = CH, J1 8.9, J2 2.3 Hz, C_6H_4); 7.99 d (1H, = CH, J 8.9 Hz, C_6H_4); 8.18-8.23m (2H, C_6H_3Br); 8.46 s (1H, = CH quin); 9.03d (1H, = CH, J 2.3 Hz, C_6H_3Br,); 11.30 s (2H, NH and SH). ^{13}C: 55.3 ($^{18}CH_3$); 114.9 (CH); 114.9 (CH); 121.8 (CH); 129.7 (CH); 129.7 (CH); 132.1 (CH); 132.5 (CH); 133.2 (CH); 119.6 (C); 129.2 (C); 136.9 (C); 140, 8 (C); 145.5 (C); 156.8 (C); 159.1 (C); 147.8 and 168.3 (C^{17} and C^{16} triazole). Found, %: C 52.30; H 3.15; Br 19.31; N 13.54; S 7.73. $C_{18}H_{13}BrN_4OS$. Calculated, %: C 52.31; H 3.17; Br 19.33; N 13.56; S 7.76.

Synthesis of 5-[2-(4-substituted phenyl)quinolin-4-yl]-1,3,4-thiadiazol-2-amines (10a-e). (General methodology). A mixture of thiosemicarbazide 3.22 *g* (0.01 *mol*), 2-substituted phenyl-4-quinoline carboxylic acid (0.01 *mol*) and 25 *ml* of $POCl_3$ phosphorus oxychloride is heated with stirring for 24 hours. The mixture is cooled and finely ground ice is added to the flask with vigorous stirring. The precipitated crystalline product is filtered off, dried and recrystallized from ethanol.

5-(2-Phenylquinolin-4-yl)-2,3-dihydro-1,3,4-thiadiazol-2-amine(10a). Yield 44%, mp 210-213°C, Rf 0.61. IR spectrum, υ, cm^{-1}: 3441 (NH_2). ^{1}H NMR, spectrum, d, ppm: 7.42-7.56 m (3H, C_6H_5); 7.56-7.64 m (1H, = CH, C_6H_4); 7.71-7.79 m (1H, = CH, C_6H_4); 8.12 d (1H, = CH, C_6H_4, J1 8.5 Hz); 8.22-8.30 m (2H, C_6H_5); 8.45 s (1H, = CH_2 quin); 8.82 d (1H, = CH, J 8.5 Hz, C_6H_4); 5.64 s (2H, NH and SH). ^{13}C: 118.8 (CH); 126.7 (CH); 126.7 (CH); 127.1 (CH); 129 (CH); 129.6.1 (CH); 129.6 (CH); 132.4 (CH); 134.3 (CH); 136.4 (CH); 130.5; 139.3; 142.7; 145.2; 157.4; 148.9 and 165.3 (C^{17} and C^{16} thiadiazole). Found, %: C 67.05; H 3.94; N, 18.40. $C_{17}H_{14}N_4S$. Calculated, %: C 66.64; H 4.61; N 18.29; S 10.47.

5-[2-(4-Chlorophenyl)quinolin-4-yl]-2,3-dihydro-1,3,4-thiadiazol-2-amine (10b). Yield 42%, mp 261-263°C, Rf 0.63. IR spectrum, υ, cm^{-1}: 3440 (NH2). ^{1}H NMR, spectrum, d, ppm:7.41-7.53 m (3H, C_6H_4CI); 7.58 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 7.73 ddd (1H, J = 8.5, 6.9, 1.3, C_6H_4); 8.10 dd (1H, J = 8.5, 1.3, C_6H_4); 8.22-8.27 m (1H, C_6H_4CI); 8.45 s (1H, = CHquin); 8.81 dd (1H, J = 8.5, 1.3, C_6H_4); 11.35 s (2H, NH and SH). ^{13}C: 118.8 (CH), 127.2; 129.8 (CH); 129.8 (CH); 130.8 and 130.8 (CH, C_6H_4-p); 132.2 (CH); 134.3. (CH); 136.4 (CH); 130.5 (C); 139.3 (C); 136.7 (C); 139.8 (C); 145.2 (C); 157.6 (C); 148.9 and 165.3 (C^{17} and C^{16} thiadiazole). Found, %: C 60.25; H 3.24; N, 16.50; S 9.44. $C_{17}H_{13}ClN_4S$. Calculated, %: C 59.91; H 3.84; Cl 10.40; N 16.44; S 9.41.

5-[2-(4-Bromophenyl)quinolin-4-yl]-2,3-dihydro-1,3,4-thiadiazol-2-amine (10c). Yield 44%, mp 278-280°C, Rf 0.61. IR spectrum, υ, cm^{-1}: 3398 (NH_2). ^1H NMR, spectrum, d, ppm: 7.46-7.53 m (2H, C_6H_4); 7.60 dd (1H, = CH, J1 8.5, J2 6.9, J3 1.3 Hz, C_6H_4Br); 7.74 dd (1H, = CH,J1 8.5, J2 6.9, J3 1.3 Hz, C_6H_4 Br); 8.11 d (1H, = CH, J1 8.5, J2 1.3 Hz, C_6H_4Br); 8.24-8.30m (2H, C_6H_4); 8.43 s (1H, = CHquin); 8.81 dd (1H, = CH, J1 8.5, J2 1.3 Hz, C_6H_4Br); 4.61s (SH, NH). ^{13}C: 118.8 (CH), 127.2; 129.8 (CH); 129.8 (CH); 131. 3 and 131.3 (CH, C_6H_4-p); 132.2 (CH); 134.3. (CH); 136.4 (CH); 122.9 (C); 130.5 (C); 133.4 (C); 139.3 (C); 140.2 (C); 145.2 (C); 158.6 (C); 148.9 and 165.3 (C^{17} and C^{16} thiadiazole). Found, %: C 53.22; H 2.81; N 14.56. $C_{17}H_{13}BrN_4S$. Calculated, %: C 53.00; H 3.40; Br 20.74; N 14.54; S 8.32.

5-[2-(4-Methoxyphenyl)quinolin-4-yl]-2,3-dihydro-1,3,4-thiadiazol-2-amine (10e). Yield 48%, mp 243°C, Rf 0.61. IR spectrum, υ, cm^{-1}: 3438 (NH_2). ^1H NMR, spectrum, d, ppm: 3.88c (3H, OCH_3); 7.46-7.53 m (2H, C_6H_4); 7.60 dd (1H, = CH, J1 8.5, J2 6.9, J3 1.3 Hz, $C_6H_4OCH_3$,); 7.74 dd (1H, = CH, J1 8.5, J2 6.9, J3 1.3 Hz ,C_6H_4 OCH_3); 8.11 d (1H, = CH, J1 8.5, J2 1.3 Hz, $C_6H_4OCH_3$); 8.24-8.30m (2H, C_6H_4); 8.43 s (1H, = CHquin); 8.81 dd (1H, = CH, J1 8.5, J2 1.3 Hz, $C_6H_4OCH_3$); 4.61s (SH, NH). ^{13}C: 55.3 ($18CH_3$), 114.9 (CH), 114.9 (CH), 118.6 (CH), 127.2 (CH), 130.2 (CH), 132.2 (CH), 134.3 (CH), 136.4 (CH); 130.5 (C); 135.8 (C); 139.3 (C); 145.2 (C); 158 (C); 159.1 (C); 148.9 and 165.3 (C^{17} and C^{16} thiadiazole). Found, %: C 64.23; H 4.76; N 16.64; S 9.51. $C_{18}H_{16}N_4OS$. Calculated, %: C 64.26; H 4.79; N 16.65; S 9.53.

5-[6-Bromo-2-(4-methoxyphenyl)quinolin-4-yl]-2,3-dihydro-1,3,4-thiadiazole-2-amine (10e). Yield 48%, mp 281-283°C, Rf 0.63. IR spectrum, υ, cm^{-1}: 3445 (NH_2). ^1H NMR, spectrum, d, ppm: 3.88c (3H, OCH_3); 7.46-7.53 m (2H, C_6H_3Br); 7.60 dd (1H, = CH, J1 8.5, J2 6.9, J3 1.3 Hz, $C_6H_4OCH_3$); 7.74 dd (1H, = CH, J1 8.5, J2 6.9, J3 1.3 Hz, C_6H_4 OCH_3); 8.11 d (1H, = CH, J1 8.5, J2 1.3 Hz, $C_6H_4OCH_3$); 8.24-8.30m (1H, C_6H_3Br); 8.43 s (1H, = CHquin); 8.81 dd (1H, = CH, J1 8.5, J2 1.3 Hz ,$C_6H_4OCH_3$); 4.61 s. (SH, NH). ^{13}C: 55.3 ($1CH_3$), 114.9 (CH), 114.9 (CH), 119.8 (CH), 130.2 (CH), 130.2 (CH), 132.2 (CH), 132.8 (CH), 133.2 (CH); 120.4 (C); 131.2 (C); 135.8 (C); 140 (C); 157.5 (C); 159.1 (C); 148.9 and 165.3 (C^{17} and C^{16} thiadiazole). Found, %: C 52.00; H 3.62; Br 19.21; N 13.46; S 7.70. $C_{18}H_{15}BrN_4OS$. Calculated, %: C 52.06; H 3.64; Br 19.24; N 13.49; S 7.72.

Synthesis of N1-[5-(2-substituted phenyl-6-substituted-quinolin-4-yl)-1,3,4-thiadiazol-2-yl]acetamides (11a-e). (General methodology). To (0.01 *mol*) of the substituted 1,3,4-thiadiazole-2-amine **(10a-e**), 10 *ml* of acetic anhydride and 2 *ml* of acetic acid are added, heated for 3 hours. After distillation of acetic anhydride, 15 *ml* of a 15% NaOH solution is added to a pH of 7-8. The crystalline substance is filtered off, washed repeatedly with water, dried, recrystallized from ethanol.

N-[5(2-phenyl-4-quinoline)-1,3,4-thiadiazol-2-yl]acetamide (11a). Yield 74%, mp 241-243°C, Rf 0.58. IR spectrum, υ, cm^{-1}: 3245 (NH), 1668 (NH-C = O). ^{1}H NMR, spectrum, d, ppm: 2.34 s (3H, CH_3); 7.20 m (1H, = CH, C_6H_5); 7.98-7.99 m (2H, = CH, C_6H_4); 7.73m (1H, = CH, C_6H_4); 7.76 m (1H, = CH, C_6H_4); 7.18 d (2H, = CH, C_6H_5): 7.75 d (2H, = CH, C_6H_5): 8.71 s (1H, = CHquin.); 11.33 s (1H, NH). ^{13}C: 23.2 (CH_3); 117.8 (CH); 126.7 (CH); 126.7 (CH); 127.1 (CH); 129.0 (CH); 129.6 (CH); 129.6 (CH); 132. 3 (CH); 134.3 (CH); 134.9 (CH); 133.1 (C); 140.9 (C); 142.7 (C); 146.8 (C); 156.9 (C); 170.9 (C); 148.9 and 165.3 (C^{17} and C^{16} thiadiazole). Found, %: C 65.80; H 4.04; N, 16.10; S9.21. $C_{19}H_{14}N_4OS$. Calculated, %: C 65.88; H 4.07; N 16.17; S 9.26

N1-5-[2-(4-Chlorophenyl)-4-quinoline]-1,3,4 thiadiazol-2-yl-acetamide (11b). Yield 67%, mp 251-253°C, Rf 0.54. IR spectrum, υ, cm^{-1}: 3315 (NH), 1667 (NH-C = O). ^{1}H NMR, spectrum, d, ppm: 2.34 s (3H, CH_3); 7.20 m (1H, = CH, C_6H_4); 7.98-7.99 m (2H, = CH, C_6H_4); 7.73m (1H, = CH, C_6H_4); 7.76 m (1H, = CH, C_6H_4); 7.10 d (2H, = CH, C_6H_4CI): 7.81 d (2H, = CH, C_6H_4CI): 8.66 s (1H, = CHquin.); 11.33 s (1H, NH). ^{13}C: 23.2 ($C^{18}H_3$); 117.8 (CH); 127.2 (CH); 129.7 (CH); 129.7 (CH); 130.8 (CH); 130.8 (CH); 132.2 (CH); 134.3 (CH); 134.9 (CH); 133.1 (C); 133.4 (C); 139.7 (C); 140.9 (C); 146.8 (C); 156.9 (C); 170.9 (C); 149.3 and 159.3 (C^{17} and C^{16} thiadiazole). Found, %: C 60.25; H 3.24; N 16.50; S 9.44. $C_{17}H_{11}ClN_4S$. Calculated, %: C 60.27; H 3.27; Cl 10.46; N 16.54; S 9.46.

N1-5-[2-(4-Bromophenyl)-4-quinoline]-1,3,4-thiadiazol-2-yl-acetamide (11c). Yield 50.45%, mp 210-213°C. Rf 0.63. IR spectrum, υ, cm^{-1}: 3317 (NH), 1668 (NH-C = O). ^{1}H NMR, spectrum, d, ppm: 2.34 s (3H, CH_3); 7.20 m (1H, = CH, C_6H_4); 7.98-7.99 m (1H, = CH, C_6H_4); 7.73m (1H, = CH, C_6H_4); 7.76 m (1H, = CH, C_6H_4); 8.66 s (1H, = CHquin.); 7.10 d (2H, = CH, C_6H_4Br); 7.81 d (2H, = CH, C_6H_4Br); 11.32s (1H, NH). ^{13}C: 23.2 ($^{18}CH_3$); 117.8 (CH); 127.2 (CH); 129.7 (CH); 129.7 (CH); 131.8 (CH); 131.8 (CH); 132.2 (CH); 134.3 (CH); 134.9 (CH); 122.9 (C); 133.1 (C); 140.2 (C); 140.9 (C); 146.8 (C); 157.2 (C); 170.9 (C); 149.3 and 159.3 (C^{17} and C^{16} thiadiazole). Found, %: C53.25; H 2.84; Br 20. 81; N 14.52; S 8.34. $C_{17}H_{11}BrN_4S$. Calculated, %: C 53.28; H 2.89; Br 20. 85; N 14.62; S 8.36.

N1-5-[2-(4-methoxyphenyl)-4-quinoline]-1,3,4-thiadiazol-2-yl-acetamide (11e). Yield 50%, mp 228-230°C, Rf 0.64. IR spectrum, n, cm^{-1}: 3260 (NH), 1668 (NH-C = O). ^{1}H NMR, spectrum, d, ppm: 2.34 s (3H, CH_3); 3.70c (3H, OCH_3); 7.98-7.99 m (2H, = CH, C_6H_4); 7.73 dd (1H, = CH, J1 8.9, J2 2.3 H, C_6H_4); 7.76m (1H, = CH, C_6H_4); 8.75 s (1H, = CH quin); 6.98m (2H, = CH, $C_6H_4OCH_3$); 7.87m (2H, = CH, $C_6H_4OCH_3$); 11.32 s (1H, NH). ^{13}C: 23.2 ($^{18}CH_3$); 55.3 ($^{18}CH_3$); 114.9 (CH); 114.9 (CH); 117.6 (CH); 127.1 (CH); 130.1 (CH); 130.1 (CH); 132.2 (CH); 134.3 (CH); 134.9 (CH); 133.1 (C); 135.8 (C); 140.2 (C); 146.8 (C); 156.5 (C); 159.1 (C); 170.9 (C); 149.3 and 159.3 (C^{17} and C^{16} thiadiazole). Found, %: C 52.30; H 3.14; N

13.51; S 7.72. $C_{18}H_{13}BrN_4O$ S. Calculated, %: C 52.31; H 3.17; Br 19.33; N 13.56; S 7.76.

N1-5-[6-Bromo-2-(4-methoxyphenyl)-4-quinoline]-1,3,4-thiadiazole-2-yl-acetamide (11e). Yield 49%, mp 241-243°C, Rf 0.63. IR spectrum, υ, cm^{-1}: 3260 (NH), 1667 (NH-C = O). ^{1}H NMR, spectrum, d, ppm: 2.34 s (3H, CH_3); 3.70c (3H, OCH_3); 7.23m (1H, = CH, C_6H_3Br); 7.70 dd (1H, = CH, J1 8.9, J2 2.3 Hz, C_6H_3Br); 8.62 m (1H, = CH, C_6H_3Br); 8.75s (1H, = CH quin); 6.98m (2H, = CH, $C_6H_4OCH_3$); 7.87m (2H, = CH, $C_6H_4OCH_3$); 11.32 s (1H, NH). ^{13}C: 23.2 ($^{18}CH_3$); 55.3 ($^{18}CH_3$); 114.9 (CH); 114.9 (CH); 118.8CH); 130.1 (CH); 130.1 (CH); 131.1 (CH); 132.7 (CH); 132.8 (CH); 120.4 (C); 133.8 (C); 135.8 (C); 140.4 (C); 145.7 (C); 156.2 (C); 159.1 (C); 170.9 (C); 149.3 and 159.3 (C^{17} and C^{16} thiadiazole). Found, %: C 52.30; H 3.14; N 13.51; S 7.72. $C_{18}H_{13}BrN_4OS$. Calculated, %: C 52.31; H 3.17; Br 19.33; N 13.56; S 7.76.

2-R-6R'-4-ՔԻՆՈԼԻՆ ԿԱՐԲՈՆԱԹԹՎԻ ՀԵՏԱՐԻԼ ՔԻՆՈԼԻՆՆԵՐԻ ՇԱՐՔԻ ՆՈՐ ԱԾԱՆՑՅԱԼՆԵՐԻ ՍԻՆԹԵԶԸ

Ա. Ն. ԻՍԱԽԱՆՅԱՆ , Գ. Ա. ԳԵՎՈՐԳՅԱՆ, Ն. Մ. ՍՏԵՓԱՆՅԱՆ, Ա. Գ. ԱՌԱՔԵԼՅԱՆ, Ա. Ս. ՍԱՖԱՐՅԱՆ և Ա. Ա. ՇԱԽԱՏՈՒՆԻ

2-Տեղակալված քինոլին-4-կարբոնաթթուների թիոսեմիկարբազիդների ներմոլեկուլային հետերոցիկլացման արդյունքում հիմնային և թթվային միջավայրում ստացվել են հետարիլ քինոլինների շարքի տրիազոլային և թիադիազոլային ցիկլեր պարունակող 2-տեղակալված քինոլին-4-կարբոնաթթուների նոր ածանցյալներ: Համապատասխան 1,3,4-թիադիազոլ-2-ամինների ացիլացումը բերել է 2,6-տեղակալված քինոլին-4-կարբոնաթթուների 1,3,4-թիադիազոլ-2-ացետամիդների ստացմանը: Բոլոր սինթեզված միացությունները պոտենցիալ կենսաբանորեն ակտիվ միացություններ են և նրանց նկատմամբ հետագա ուսում նասիրությունները կշարունակվեն:

СИНТЕЗ НОВЫХ ПРОИЗВОДНЫХ 2-R-6R'-4-ХИНОЛИНКАРБОНОВЫХ КИСЛОТ ИЗ РЯДА ГЕТАРИЛ ХИНОЛИНОВ

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В результате внутримолекулярной гетероциклизации тиосемикарбазидов 2-замещенных хинолин-4-карбоновых кислот в щелочной и кислой среде выделены новые производные 2-замещенных хинолин-4-карбоновых кислот, содержащие триазоловые и тиадиазоловые циклы – соединения из ряда гетарилхинолинов. Ацилированием соответствующих 1,3,4-тиадиазол-2-аминов получены 1,3,4-тиадиазол-2-ил-ацетамиды-2,6-замещенных-4-хинолинкарбоновых кислот. Все синтезированные соединения являются потенциально биологически активными соединениями, и дальнейшее изучение их активности является перспективным.

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