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# THE EFFICIENT SYNTHESIS OF 3-R-6-THIO-6,7-DIHYDRO-2*H*-[1,2,4]TRIAZINO[2,3-*c*]-QUINAZOLINE-2-ONES AND THEIR DERIVATIVES, ANTIMICROBIAL AND ANTIFUNGAL ACTIVITY

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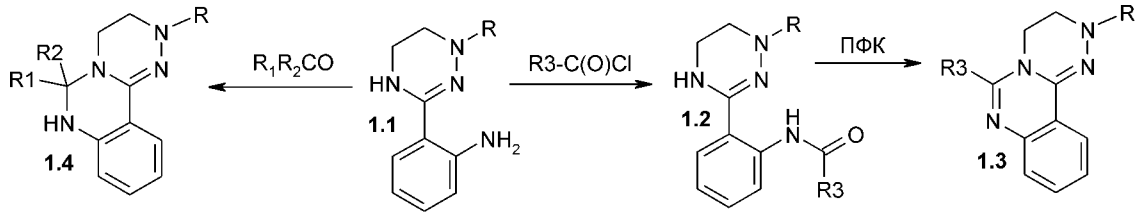
***The reaction of 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones (2) with carbon bisulphide leads to formation of potassium salts of 3-substituted 6-thio-6,7-dihydro-2H-[1,2,4]triazino[2,3-c]quinazoline-2-ones in the presence of potassium hydroxide or its "synthetic equivalent" potassium ethylxanthogenate in alcohols. Their alkylation with chloracetic acid snd its sunstituents occurs regioselectively. The structure of the compounds synthesized was confirmed by spectral data and X-ray diffraction analysis. The antimicrobial and antifungal activity of the compounds synthesized was tested against Escherichia coli, Aspergillus niger, Mycobacterium luteum, Candida albicans and Candida tenuis.***

***ЕФЕКТИВНИЙ СИНТЕЗ 3-R-6-ТІО-6,7-ДИГІДРО-2Н-[1,2,4]ТРИАЗИНО[2,3-c]-ХІНАЗОЛІН-2-ОНІВ ТА ЇХ ПОХІДНИХ, АНТИБАКТЕРІАЛЬНА ТА АНТИФУНГІЦИДНА АКТИВНІСТЬ***
***Г.Г.Берест, О.Ю.Воскобойнік, С.І.Коваленко, Р.С.Синяк, І.В.Омельченко, О.В.Шишкін, О.З.Комаровська-Порохнявець, В.П.Новиков***
***Реакція 6-R-3-(2-амінофеніл)-1,2,4-триазин-5-онов (2) з сірковуглецем в етанолі у присутності калію гідроксиду або його "синтетичного еквіваленту" — калію етилксантогенату у спиртах призводить до утворення калієвих солей 3-заміщених 6-тіо-6,7-дигідро-2Н-[1,2,4]триазино[2,3-c]хіназолін-2-онів. Алкілування калієвих солей 3-R-6-тіо-6,7-дигідро-2Н-[1,2,4]триазино[2,3-c]хіназолін-2-онів хлороцтовою кислотою та її заміщеними проходить S-регіоселективно. Структура синтезованих сполук підтверджена спектральними і рентгеноструктурними методами аналізу. Антибактеріальна і антифунгіцидна активність синтезованих сполук вивчена на Escherichia coli, Niger Aspergillus, Mycobacterium luteum, Candida albicans і Candida tenuis.***

***ЭФФЕКТИВНЫЙ СИНТЕЗ 3-R-6-ТИО-6,7-ДИГИДРО-2Н-[1,2,4]ТРИАЗИНО[2,3-c]-ХИНАЗОЛИН-2-ОНОВ И ЕГО ПРОИЗВОДНЫХ, АНТИБАКТЕРИАЛЬНАЯ И АНТИФУНГИЦИДНАЯ АКТИВНОСТЬ***
***Г.Г.Берест, А.Ю.Воскобойник, С.И.Коваленко, Р.С.Синяк, И.В.Омельченко, О.В.Шишкин, Е.З.Комаровская-Порохнявец, В.П.Новиков***
***Реакция 6-R-3-(2-аминофенил)-1,2,4-триазин-5-онов (2) с сероуглеродом в этаноле в присутствии калия гидроксида или его "синтетического эквивалента" — калия этилксантогената в спиртах приводит к образованию калиевых солей 3-замещенных 6-тио-6,7-дигидро-2Н-[1,2,4]триазино[2,3-c]хиназолин-2-онов. Алкилирование калиевых солей 3-R-6-тио-6,7-дигидро-2Н-[1,2,4]триазино[2,3-c]хиназолин-2-онов хлоруксусной кислотой и ее замещенными проходит S-региоселективно. Структура синтезированных соединений подтверждена спектральными и рентгеноструктурным методами анализа. Антибактериальная и антифунгицидная активность синтезированных соединений изучена на Escherichia coli, Niger Aspergillus, Mycobacterium luteum, Candida albicans и Candida tenuis.***

Methods of synthesis of the [1,2,4]triazino[4,3-*c*]quinazoline systems and their isomer [2,3-*c*]-seria comes to the successive building-up of pyrimidine and triazin heterocycles [1, 2] formation of triazine heterocycle on quinazoline framework [3-9] or pyrimidine heterocycle on triazin framework [10-13]. The last way provides possibility of synthesis of 6-mono (1.3) and 6-disubstituted (1.4) of [1,2,4]triazino[4,3-*c*]quinazoline by the treatment of 1-alkyl-3-(2-aminophenyl)-1,4,5,6-tetrahydro-[1,2,4]triazines (1.1) with




R=Alk; R1=H, Alk; R2=Alk, Ar, Het; R3=Ph, 2-F-Ph, 4-F-Ph, 4-MePh, 4-NCPh, 3-BrPh, 4-BrPh, 3,4,5-$(OMe)_3$Ph, 3,4-$Cl_2$Ph

Scheme 1

aliphatic, aromatic and heterocyclic aldehydes and ketones, aromatic or heterocyclic acids chloroanhydrides (Scheme 1).

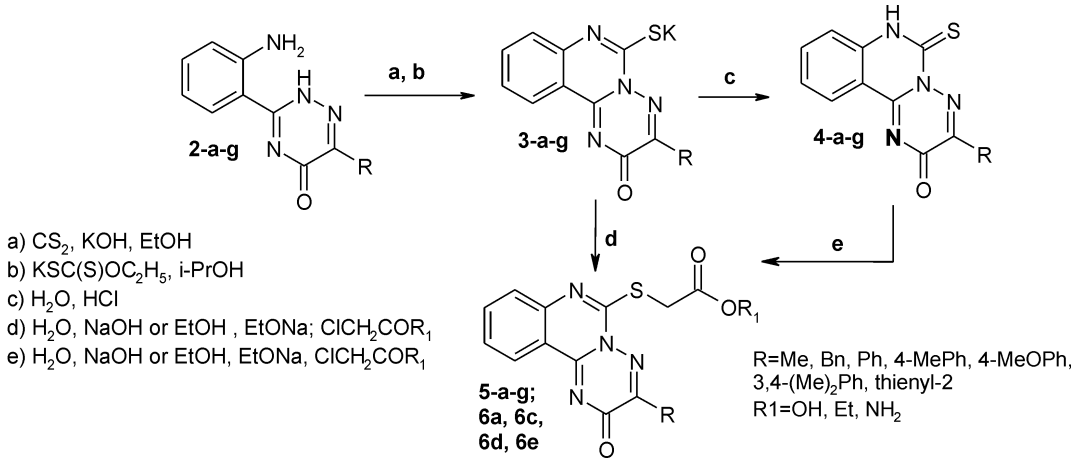
Proceeding with the research of development the insufficiently known heterocyclic systems, namely [1,2,4]triazino[2,3-*c*]quinazolines and their isomer [4,3-*c*]-seria [6, 8, 9], we have investigated reactivity of 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ons to some dielectrophils. A fortiori, 6-substituted triazinoquinazolines have shown antidepressive, anorectic, anti-inflammatory, analgetic, antibacterial and other types of activity [1, 2, 5, 10-21].

6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones (**2**) — 1,5-NCCCN binucleophils, which due to the presence of amide bond are inclined to imido-imidolic tautomerism and can exist in two tautomeric forms: 2*H* (**A**) and 4*H* (**B**). Consequently, after heterocyclisation both S-triazino[2,3-*c*]quinazolines and their isomer [4,3-*c*]-seria could possible be obtained. So, investigation of the reaction of 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones (**2**) with dielectrophils, namely carbon bisulphid and it's "synthetic equivalent" potassium xantogenate was in fact interestingly.

Synthesis of potassium salts 3 was conducted by two methods: firstly, by treatment of compounds 2 with carbon bisulphid in ethanol in presence of potassium hydroxide (method A), secondly, by interaction of compounds 2 with potassium xantogenate in the propanol-2 (method B, Chart 2). In the result it was shown that the last method of synthesis had several advantages: simplicity of conduction, high yields and purity of products. The proper potassium salts 3 were converted into thions 4 by addition of hydrochloric acid to pH 3-4 in water solution to confirm their structure (Scheme 2).

Alkylation of potassium salts **3** by chloracetic acid and its substituted went smoothly with formation of acids **5**, esters **6** and amides 7 in ethanol or aqueous-ethanolic solution in presence of basic reagents (Chart 3). Compounds **5, 6** were also derived by alkylation of proper thions **4** (Scheme 2). In addition, esters **6** were got by the oncoming synthesis, namely, esterefication in the conditions of acid catalysis (method A) and in the presence of thionylchloride (method B). It was necessary to notice that the last method provided quantitative yields and was more convinient in realization. We didn't succeed in getting amides 7 by the aminolysis of the proper ethers **6** because of law electrophilic properties of carboxyl group.

The structure of thions **4** was proved by the element analysis and spectral data. In the LC-MS specta of thions **4** the positive ions $[M+1]^+$ and $[M+3]^+$ were registered, characterizing "isotopic shape" of sulphur and confirming the expected molecular weight of compounds **4**. In $^1$H NMR spectra of compounds **4** the law field singlet of protons of thioamide group was registered at 13.96-13.83 ppm., and signals of triazinoquinazoline protons were shown with the proper chemical shifts and multiplicity (H-11 (d), H-9 (t), H-10 (d) and H-8 (d)) [8, 9]. Appearance in $^{13}$C NMR spectra of compounds **4** characteristic signals of decoupled atoms of C-6 at 171.05-168.79 ppm con-




Scheme 2

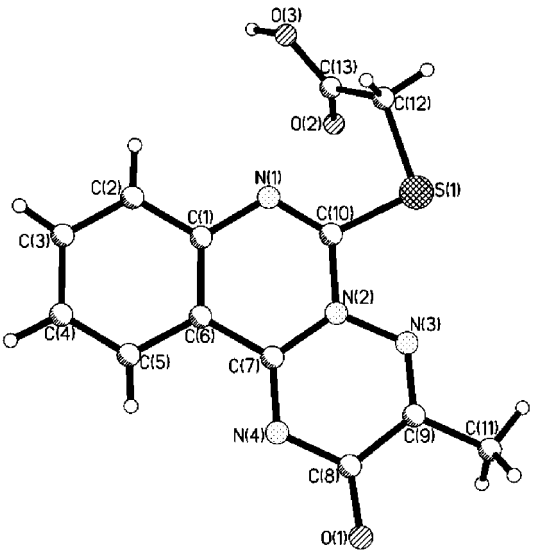



Fig. Structure of 5a according to X-ray diffraction data.

firmed the formation of the new heterocyclic system, and also considerably differentiated them from substrates 2 [22].

LC-MS spectra of compounds **5, 6** and 7 were characterised by the positive ions $[M+1]^+$ and $[M+3]^+$, and some of them (**5d, 5f**) — by fragment ion $[M—CH_2COOH]^+$. In $^1H$ NMR spectra of compounds **5, 6** и **7** besides signals of triazinoquinazoline cycle, there were S-$CH_2$-group signals at 4.14-3.96 ppm. It's important that for compound 6 the signal of the mentioned proton was overlapped by the quadruplet of $CH_2$ of ester group. Law field singlet of carboxyl group was registered at 13.92-12.89 ppm for compounds **5**, and for compounds **7** — the nonequivalent propons of $NH_2$-group: singlet at 7.30-7.17 ppm and singlet in the multiplet at 7.78-7.52 ppm (H-8, H-10). $^{13}C$ NMR spectra of compounds **5**, unlike to thions **4**, showed high field shift of signal C-6 to 150.66-154.41 ppm, S-$CH_2$ group at 34.22-34.21 ppm., and signal carboxyl group at 170.08-170.04 ppm.

Mass spectra (EI) of the thiones **4** had it's own features and considerably differed from the spectra of other heteroaromatic sulfides. In this case, fragmentation of molecular ion [M+] under the electron impact initially took place by bonds C(2) — C(3) and N(3) — N(4) with splitting off the nitryl radical (R-CN) and formation of ion with *m/z* 203, having highest intensity in a spectrum (100-96,7%). Consequently, a triazine cycle was exposed to destruction, and, that was important, localization of positive charge was traced on thiobenzpyrimidine cycle. And so for $[M]^+$ (*m/z* 203) there was rejection of S, SH, CNS, CHNS and CNO radicals with formation of ions with *m/z* 171, 170, 161, 145, 144 with proper intensities in a spectrum.

MS (EI) of acids **5**, unlike to thions **4**, had it's peculiarities. So, first fragmentation stage of [M+] the π-deficite heteroaromatic system was carried out by bonds C(2) — C(3) and N(3) — N(4) with localization of positive charge on a fragment $[R\text{-}CN]^+$, with the greater degree of it's delocalization, and by formation of the supposed fragment with *m/z* 261. The last one eliminated particles of $CO_2$, COOH and $SCH_2COOH$ with formation of high-intensive fragmentation ions with *m/z* 217 (100-75.1%), 216 (88.8-20.0%) and 171 (100-48.6%) accordingly. The second direction fragmentation was related to formation of ions $[M—CH_2COOH]^+$ with *m/z* 243 (**5a**), 319 (**5b**), 305 (**5c**), 319 (**5d**), 335 (**5e**), 333 (**5f**) and by destruction $[M—C_2COOH]^+$ by bonds C(2) — C(3) and N(3) — N(4). The fragmentary ions formed in first and second case ejected the easy going radicals ($CH_3$, S, CS, CNS and CNO) with formation of peaks with *m/z* 203, 185, 171, 160, 159, 145, 129 with the proper intensity in a spectrum. Fragmentation of ethers **6** in MS (EI) was similar to the proper acids **5**. An exception was ether **6d** with emission of radical S from a fragmentary ion (*m/z* 218) and formation of peak with *m/z* 186 with maximal intensity in a spectrum.

The spectral data and characteristics of the 6-thio-S-triazinoquinazoline system in MS (EI) didn't allow simply to differentiate [4,3-*c*]- and [2,3-*c*]-isomeric systems. For definite confirmation of structure of the synthesized compounds X-ray diffraction study of compound **5a** was performed (Fig.). Quinazoline fragment is a planar within 0.016 A°, Triazine ring has slightly non-planar conformation (the N(3)—C(9)—C(8)—N(4) torsion angle is 6.1(2)°). In spite of π-π conjugation within bicyclic fragment, the N(1)=C(10) (1.278(2) A°) and N(3)=C(9) (1.283(1) A°) bonds are slightly shortened, and N(2)—C(10) (1.401(1) A°) bond is elongated as compare to their mean values [23] for isolated heterocycles (1.313 A°-1.376 A°, correspondingly). Carboxylic group plane is turned with respect to the average plane of tricyclic fragment (the C(10)—S(1)—C(12)—C(13) torsion angle is — 66.0(1)°). In the crystal, molecules forms centrosymmetric dimers due to strong intermolecular hydrogen bonds between carboxylic groups: O(3—H(3O)...O(2)' (-x,-y, -z+2) H:O' 1.51(2) A°, C-H:O' 175(2)°. These dimers are organized in double chains along (100) crystallographic direction by the stacking interaction (distance between the planes of tricyclic fragments of neighboring molecules is 3.46 A°).

Thus, the complex of physical and chemical investigations proved that 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ons (2) in the reaction of heterocyclisation with carbon bisulphid or potassium ethylxantoganate formed 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-2-ones.

Biological tests of all compounds which were synthesized showed that most of them demonstrated an antifungal activity against *Aspergillus niger*. It should be noted that antifungal action against *Aspergillus niger* were characteristic for correspondent [(3-R-2-oxo-*2H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic acids (**5**), their esters (**6**) and amides (**7**). Whereas only some potassium salts (**3d, 3f, 3g**) and thiones (**4d, 4g**) were active according to *Aspergillus niger*. We noted

that thiones (**4a, 4b, 4c**) and their potassium salts (**3a, 3b, 3c, 3d, 3f**) displayed antimicrobial activity against *Mycobacterium luteum*, which were comparable to "Nystatine". Among the derivatives **5-7** only [(3-phenyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]-acetic acid amide (**7c**) displayed an activity against *Mycobacterium luteum*. Practically all investigated compounds were inactive according to *Escherichia coli, Candida tenuis* and *Staphylococcus aureus.* 3-Phenyl- (**3c**) and 3-(4′-methylphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4]-triazino[2,3-*c*]guinazoline-2-ones (**3d**) were exceptions and displayed higher (**3c**) or similar (**3d**) antibacterial activity against *Staphylococcus aureus* in comparison with "Vancomicin" and "Oxacillin".

## Experimental

Melting points were determined in open capillary tubes in a Thiele's apparatus and were uncorrected. IR spectra (4000-600 $cm^{-1}$) were recorded on a Bruker ALPHA FT-IR spectrometer using a module for measuring attenuated total reflection (ATR). $^{1}H$ and $^{13}C$ NMR spectra (500 MHz for $^{1}H$ and 125 MHz for $^{13}C$) were recorded on a Bruker Avance DRX-500 spectrometer with $SiMe_4$ as internal standard in DMSO-$d_6$ solution. LC-MS were recorded using chromatography/mass spectrometric system which consists of high-performed liquid chromatograph "Agi1ent 1100 Series" equipped with diode-matrix and mass-selective detector "Agi1ent LC/MSD SL" (atmospheric pressure chemical ionization — APCI). Electron impact mass spectra (EI-MS) were recorded on a Varian 1200 L instrument at 70 eV. The purity of all obtained compounds was checked by $^{1}H$ NMR and LC-MS.

6-R-3-(2-aminophenyl)-2*H*-[1,2,4]-triazin-5-on es (**2**) was synthesized according to the reported procedure [22]. Other starting materials and solvents were obtained from commercially available sources and used without additional purification.

**General Procedure for the Synthesis of Potassium 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3a-g)**

*Method A.* 0,76 g (10 mmol) of carbon bisulphid was instiled with stirring to a solution of 0,56 g (10 mmol) of potassium hydroxide in 20 ml of ethanol. Proper 3-(2-aminophenyl)-6-R-2*H*-[1,2,4]triazin-5-on (2) (10 mmol) was added to the obtained solution and refluxed for 4 hours. Resulted mixture was cooled, solid was filtered and dried.

*Method B.* 1,60 g (10 mmol) of potassium ethylxantogenate was added to the suspension of proper 3-(2-aminophenyl)-6-R-2*H*-[1,2,4]triazin-5-on (2) (10 mmol) in 20 ml of propanol-2 and refluxed for 4 hours. Resulted mixture was cooled, solid was filtered and dried.

**Potassium 3-Methyl-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3a).** Yield — 73,5% (method A), 75,8% (method B). Mp — 204-206°C. IR ($cm^{-1}$): 3407, 3290, 3063, 2984, 2909, 2842, 1621, 1566, 1520, 1472, 1430, 1379, 1337, 1298, 1264, 1239, 1210, 1166, 1150, 1030, 944, 862, 766, 735, 688, 661, 636, 614; Anal. Calcd for $C_{11}H_7N_4OSK$: C, 46.79; H, 2.50; N, 19.84; S, 11.35; Found: C, 46.78; H, 2.50; N, 19.83; S, 11.35.

**Potassium 3-Benzyl-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3b).** Yield — 99,9% (method A), 98,5% (method B). Mp — 248-250°C. IR ($cm^{-1}$): 3322, 3060, 3023, 2963, 2917, 2873, 2848, 1649, 1604, 1584, 1569, 1531, 1479, 1467, 1451, 1434, 1393, 1373, 1347, 1294, 1271, 1236, 1212, 1171, 1148, 1123, 1066, 1031, 1020, 1000, 948, 926, 863, 841, 818, 764, 750, 692, 642; Anal. Calcd for $C_{17}H_{11}N_4OSK$: C, 56.96; H, 3.09; N, 15.64; S, 8.95; Found: C, 56.95; H, 3.09; N, 15.66; S, 8.94.

**Potassium 3-Phenyl-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3c).** Yield — 55,3% (method A), 80,9% (method B). Mp > 310°C. IR ($cm^{-1}$): 1620, 1602, 1570, 1524, 1493, 1474, 1463, 1432, 1371, 1345, 1319, 1296, 1277, 1253, 1232, 1171, 1155, 1077, 1034, 1001, 985, 939, 856, 818, 755, 695, 656, 606; Anal. Calcd for $C_{16}H_9N_4OSK$: C, 55.79; H, 2.63; N, 16.27; S, 9.31; Found: C, 55.78; H, 2.65; N, 16.27; S, 9.31.

**Potassium 3-(4′-Methylphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3d).** Yield — 76,9% (method A), 77,4% (method B). Mp > 310°C. IR ($cm^{-1}$): 3079, 1620, 1602, 1570, 1524, 1477, 1463, 1433, 1405, 1371, 1346, 1320, 1300, 1278, 1246, 1233, 1172, 1112, 1075, 1035, 1023, 985, 939, 874, 855, 835, 798, 783, 755, 715, 695, 684, 660, 641, 629, 611; Anal. Calcd for $C_{17}H_{11}N_4OSK$: C, 56.96; H, 3.09; N, 15.64; S, 8.95; Found: C, 56.94; H, 3.09; N, 15.65; S, 8.94.

**Potassium 3-(4′-Methoxyphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3e).** Yield — 95,9% (method A), 98,9% (method B). Mp > 310°C. IR ($cm^{-1}$): 2963, 2904, 2830, 1650, 1601, 1570, 1536, 1505, 1477, 1439, 1417, 1368, 1343, 1315, 1297, 1280, 1261, 1254, 1232, 1168, 1133, 1075, 1029, 1018, 1008, 984, 939, 857, 837, 819, 800, 754, 724, 705, 689, 657, 635, 625, 611; Anal. Calcd for $C_{17}H_{11}N_4O_2SK$: C, 54.53; H, 2.96; N, 14.96; S, 8.56; Found: C, 54.53; H, 2.97; N, 14.95; S, 8.55.

**Potassium 3-(3′,4′-Dimethylphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3f).** Yield — 67,2% (method A), 79,5% (method B). Mp > 310°C. IR ($cm^{-1}$): 3438, 3394, 3292, 3054, 3021, 2962, 2916, 1660, 1644, 1626, 1602, 1568, 1537, 1524, 1475, 1432, 1393, 1369, 1347, 1295, 1274, 1254, 1232, 1185, 1167, 1126, 1078, 1013, 982, 950, 903, 890, 868, 849, 833, 756, 736, 713, 704, 688, 659, 634; Anal. Calcd for $C_{18}H_{14}N_4OSK$: C, 57.88; H, 3.78; N, 15.00; S, 8.59; Found: C, 57.86; H, 3.78; N, 15.02; S, 8.59.

**Potassium 3-(Thienyl-2)-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (3g).** Yield — 63,4% (method A), 78,4% (method B). Mp — 244-246°C. IR ($cm^{-1}$): 3386, 3255, 3195, 3056, 3000, 2917, 2848, 1659, 1612, 1601, 1574, 1522, 1476, 1440, 1412, 1391, 1372, 1351, 1337, 1300, 1285, 1268, 1244, 1159, 1117, 1086, 1070, 1044, 983, 933, 853, 828, 789, 777,

738, 711, 699, 685, 638, 605; Anal. Calcd for $C_{14}H_7N_4OS_2K$: C, 47.98; H, 2.01; N, 15.99; S, 18.30; Found: C, 47.97; H, 2.03; N, 15.98; S, 18.29.

**General Procedure for the Synthesis of 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-ones (4a-g).** Potassium salt of proper 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-2-on (10 mmol) (3) was dissolved in 20 ml of water and acidified by addition of hydrochloric acid to pH 2-3. Obtained solid was filtered and dried.

**3-Methyl-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino [2,3-*c*]guinazoline-2-one (4a).** Yield — 98,6%. Mp — 254-256°C. IR (см$^{-1}$): 3118, 3056, 3029, 2954, 2917, 2849, 1767, 1743, 1687, 1637, 1616, 1594, 1564, 1519, 1471, 1455, 1421, 1381, 1360, 1322, 1303, 1277, 1257, 1225, 1169, 1128, 1111, 1039, 1025, 988, 949, 862, 771, 752, 716, 671, 655, 623; $^1$H NMR: δ=2.34 (s, 3H, $CH_3$), 7.48-7.43 (m, 2H, H-8, 10), 7.82 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.4, H-9), 8.29 (d, 1H, $J$ = 7.9, H-11), 13.83 (s, 1H, NH); $^{13}$C NMR: δ=20.04 ($CH_3$), 118.29 (11a), 127.49 (8), 130.30 (10), 136.24 (11), 141.07 (9), 144.04 (3), 150.25 (11b), 154.72 (7a), 160.16 (2), 170,1 (6); EI-MS, *m/z* ($I_{rel}$, %) = 246 (5.8), 245 (11.4), 244 ($M^{+\bullet}$, 65.5), 205 (2.1), 204 (13.4), 203 (100.0), 198 (10.2), 174 (10.2), 171 (7.4), 170 (12.4), 163 (4.0), 161 (35.4), 160 (6.7), 146 (2.8), 145 (76.7), 144 (21.1), 143 (22.5), 142 (5.8), 134 (13.6), 117 (8.6), 116 (9.0), 108 (6.9), 107 (7.7), 105 (8.8), 103 (11.3), 102 (35.9), 91 (6.1), 90 (42.7), 89 (5.3), 88 (5.1), 86 (11.1), 78 (5.0), 77 (8.9), 76 (15.5), 75 (23.4), 74 (5.1), 70 (10.7), 69 (10.5), 65 (8.5), 64 (27.5), 63 (19.8), 62 (5.9); LC-MS, *m/z* = 245 [M+1], 247 [M+3]; Anal. Calcd for $C_{11}H_8N_4OS$: C, 54.09; H, 3.30; N, 22.94; S, 13.13; Found: C, 54.07; H, 3.31; N, 22.93; S, 13.14.

**3-Benzyl-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino [2,3-*c*]guinazoline-2-one (4b).** Yield — 99,0%. Mp — 266-268°C. IR (см$^{-1}$): 3177, 3143, 3116, 3076, 3026, 2982, 2937, 1660, 1618, 1600, 1546, 1514, 1482, 1454, 1423, 1394, 1371, 1344, 1306, 1262, 1204, 1175, 1128, 1099, 1059, 967, 927, 874, 843, 818, 781, 772, 752, 701, 688, 667, 649, 609; $^1$H NMR: δ=4.05 (s, 2H, $CH_2C6H5$), 7.46-7.17 (m, 7H, H-8, 10, 2′, 3′, 4′, 5′, 6′), 7.78 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.4, H-9), 8.25 (d, 1H, $J^3$ = 7.9, $J^4$ = 1,2, H-11), 13.86 (s, 1H, NH); $^{13}$C NMR: δ=36.93 ($CH_2$), 116.03 (11a), 116.06 (8), 125.73 (10), 126.70 (11), 127.15 (4′-Ph), 128.81 (3′,5′-Ph), 129.68 (2′,6′-Ph), 136.31 (9), 136.34 (1′-Ph), 137.90 (3), 152.26 (11b), 155.24 (7a), 160.25 (2), 171.05 (6); EI-MS, *m/z* ($I_{rel}$, %) = 322 (6.5), 321 (21.6), 320 ($M^{+\bullet}$, 84.2), 205 (7.1), 204 (17.6), 203 (100.0), 174 (7.5), 171 (3.9), 170 (16.3), 163 (3.2), 162 (7.8), 161 (49.0), 160 (14.9), 146 (10.9), 145 (99.5), 144 (19.2), 143 (33.3), 134 (23.9), 129 (6.4), 118 (7.6), 117 (32.6), 116 (17.4), 103 (10.6), 102 (30.4), 91 (18.5), 90 (31.0), 89 (13.4), 85 (10.0), 83 (13.5), 77 (9.4), 76 (6.6), 75 (8.0), 65 (7.7), 64 (6.3), 63 (9.5), 51 (11.3), 50 (5.8); LC-MS, *m/z* = 321 [M+1], 323 [M+3]; Anal. Calcd for $C_{17}H_{12}N_4OS$: C, 63.73; H, 3.78; N, 17.49; S, 10.01; Found: C, 63.71; H, 3.77; N, 17.50; S, 10.01.

**3-Phenyl-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino [2,3-*c*]guinazoline-2-one (4c).** Yield — 95,9%. Mp > 300°C. IR (см$^{-1}$): 3358, 3182, 3014, 1654, 1608, 1589, 1546, 1512, 1497, 1456, 1398, 1356, 1337, 1302, 1278, 1243, 1205, 1178, 1156, 1128, 1091, 1046, 1024, 981, 943, 869, 833, 810, 776, 753, 721, 686, 632; $^1$H NMR: δ=7.61-7.42 (m, 5H, H-3′, 4′, 5′, 8, 10), 7.82 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.4, H-9), 8.36-8.20 (m, 3H, H-2′, 6′, 11,), 13.92 (s, 1H, NH); EI-MS, *m/z* ($I_{rel}$, %) = 308 (7.2), 307 (25.8), 306 ($M^{+\bullet}$, 69.9), 229 (5.1), 205 (35.2), 204 (74.2), 203 (96.7), 187 (11.1), 176 (5.8), 175 (6.3), 174 (19.1), 171 (9.6), 170 (59.5), 163 (6.4), 162 (13.9), 161 (100.0), 160 (36.6), 159 (7.7), 146 (27.2), 145 (98.6), 144 (43.2), 143 (82.0), 142 (13.8), 135 (8.0), 134 (54.3), 129 (7.3), 122 (7.3), 118 (8.0), 117 (49.2), 116 (13.9), 108 (5.0), 107 (5.4), 104 (7.4), 103 (37.1), 102 (68.7), 91 (6.8), 90 (56.3), 89 (23.1), 88 (5.7), 86 (7.1), 77 (21.6), 76 (35.4), 75 (24.1), 69 (5.9), 64 (13.2), 63 (28.6), 62 (8.6), 52 (8.3), 51 (18.2), 50 (14.9); LC-MS, *m/z* = 291, 307 [M+1], 323; Anal. Calcd for $C_{16}H_{10}N_4OS$: C, 62.73; H, 3.29; N, 18.29; S, 10.47; Found: C, 62.70; H, 3.30; N, 18.27; S, 10.46.

**3-(4′-Methylphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4] triazino[2,3-*c*]guinazoline-2-one (4d).** Yield — 85,6%. Mp > 300°C; IR (см$^{-1}$): 3560, 3171, 3112, 3065, 3014, 2975, 2927, 1647, 1618, 1603, 1573, 1548, 1518, 1506, 1483, 1454, 1395, 1364, 1345, 1307, 1268, 1248, 1195, 1182, 1160, 1149, 1108, 1081, 1026, 1014, 961, 943, 886, 869, 833, 810, 776, 753, 721, 686, 632,616; $^1$H NMR: δ=2.39 (s, 3H, $CH_3$), 7.35 (d, 2H, $J$ = 8.2, H-3′, 5′), 7.52-7.43 (m, 2H, H-8, 10), 7.82 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.4, H-9), 8.24 (d, 2H, $J$ = 8.2, H-2', 6'), 8.32 (d, 1H, $J$ = 7.9, H-11), 13.88 (s, 1H, NH); $^{13}$C NMR: δ=21.50 ($CH_3$), 110.01 (11a), 115.92 (8), 117.69 (10), 128.79 (2′,6′-Ph), 128.93 (11), 129.06 (9, 1′-Ph), 129.19 (3′,5′-Ph), 130.73 (3), 133.53 (4′-Ph), 140.24 (11-b), 150.20 (7a), 158.68 (2), 168.79 (6); EI-MS, *m/z* ($I_{rel}$, %) = 320 ($M^{+\bullet}$, 4.1), 205 (6.1), 204 (12.9), 203 (100.0), 171 (8.2), 170 (10.8), 163 (3.3), 161 (24.3), 160 (8.8), 149 (15.0), 146 (6.4), 145 (69.1), 144 (11.4), 143 (22.4), 134 (16.0), 129 (8.3), 119 (6.7), 118 (9.8), 117 (49.6), 116 (32.2), 103 (8.1), 102 (22.1), 97 (7.0), 91 (9.4), 90 (29.1), 89 (14.1), 85 (6.3), 83 (10.0), 77 (8.4), 76 (7.7), 75 (7.4), 73 (5.2), 71 (6.0), 69 (8.7), 64 (5.6), 63 (8.9), 60 (6.5), 57 (14.6), 56 (7.0), 55 (12.8), 51 (7.9), 50 (5.3), 45 (7.9), 43 (14.9), 41 (14.0); LC-MS, *m/z* = 321 [M+1], 322 [M+2]; Anal. Calcd for $C_{17}H_{12}N_4OS$: C, 63.73; H, 3.78; N, 17.49; S, 10.01; Found: C, 63.74; H, 3.79; N, 17.48; S, 10.03.

**3-(4′-Methoxyphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4] triazino[2,3-*c*]guinazoline-2-one (4e).** Yield — 92,5%. Mp — 280-282°C. IR (см$^{-1}$): 3180, 3117, 3065, 3021, 2960, 2905, 2835, 1680, 1624, 1600, 1551, 1522, 1508, 1485, 1432, 1390, 1360, 1344, 1304, 1259, 1202, 1174, 1147, 1118, 1105, 1076, 1007, 941, 868, 851, 814, 786, 772, 752, 724, 706, 693, 680, 628, 614; $^1$H NMR: δ=3.83 (s, 3H, $OCH_3$), 7.09 (d, 2H, $J$=8.8, H-3′, 5′), 7.45 (m, 2H, H-8, 10), 7.81 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.4, H-9), 8.33 (m, 3H, H-11, 2', 6'), 13.91 (s, 1H, NH);

$^{13}$C NMR: δ=55.90 ($OCH_3$), 114.35 (3′,5′-Ph), 115.81 (11a), 116.15 (8), 124.76 (10), 125.80 (11), 126.67 (1′-Ph), 131.56 (2′,6′-Ph), 136.17 (9), 137.84 (3), 148.57 (11-b), 150.88 (7a), 160.07 (2), 162.26 (4′-Ph), 171.03 (6); EI-MS, *m/z* ($I_{rel}$, %) = 336 ($M^{+\bullet}$, 7.1), 205 (5.6), 204 (11.9), 203 (100.0), 170 (9.5), 163 (3.4), 161 (25.0), 160 (7.7), 149 (6.5), 146 (6.9), 145 (69.7), 144 (11.2), 143 (24.3), 134 (21.2), 133 (47.1), 129 (7.7), 119 (11.3), 118 (7.1), 117 (19.5), 116 (5.5), 104 (6.3), 103 (20.3), 102 (20.4), 91 (6.1), 90 (29.9), 76 (9.0), 75 (6.6), 64 (7.2), 63 (8.8), 57 (5.3), 55 (6.4), 51 (5.1), 45 (8.9), 41 (6.2); LC-MS, *m/z* = 337 [M+1], 339 [M+3]; Anal. Calcd for $C_{17}H_{12}N_4O_2S$: C, 60.70; H, 3.60; N, 16.66; S, 9.53; Found: C, 60.69; H, 3.59; N, 16.64; S, 9.54.

**3-(3′,4′-Dimethylphenyl)-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-one (4f).** Yield — 93,1%. Mp > 310°C. IR (см$^{-1}$): 3246, 3192, 3119, 3070, 3033, 2969, 2923, 1674, 1656, 1618, 1551, 1535, 1516, 1499, 1483, 1447, 1389, 1343, 1305, 1258, 1220, 1188, 1144, 1131, 1107, 1083, 1030, 993, 958, 906, 868, 854, 834, 773, 756, 747, 711, 692, 682, 618; $^1$H NMR: δ=2.28 (s, 6H, 3,4-$(CH_3)_2$), 7.27 (d, 1H, $J$ = 8.1, H-5′), 7.44 (m, 2H, H-8, 10), 7.81 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.4, H-9), 8.08 (m, 2H, H-6', 2′), 8.29 (d, 1H, $J$ = 7.9, H-11), 13.9 (s, 1H, NH); $^{13}$C NMR: δ=20.00 (3-$CH_3$), 20.15 (4-$CH_3$), 115.83 (11a), 116.15 (8), 125.80 (5′-Ph), 126.73 (10), 127.38 (11), 129.95 (6′-Ph), 130.05 (3), 130.52 (9), 136.22 (2′-Ph), 136.57 (3′-Ph), 137.87 (1′-Ph), 140.55 (4′-Ph), 149.37 (11-b), 151.02 (7a), 159.98 (2), 171.05 (6); EI-MS, *m/z* ($I_{rel}$, %) = 334 ($M^{+\bullet}$, 2.8), 205 (5.7), 204 (12.0), 203 (100.0), 171 (9.4), 170 (10.2), 163 (2.1), 161 (26.5), 160 (7.2), 149 (18.0), 146 (9.1), 145 (77.9), 144 (14.5), 143 (28.3), 134 (19.7), 132 (7.3), 131 (41.0), 130 (19.7), 129 (14.9), 123 (6.6), 119 (7.0), 118 (10.4), 117 (33.3), 116 (93.0), 115 (11.5), 105 (5.9), 104 (7.9), 103 (22.3), 102 (25.2), 97 (9.3), 91 (8.7), 90 (19.5), 89 (15.3), 85 (5.8), 84 (5.1), 83 (11.3), 77 (16.1), 76 (10.5), 75 (9.9), 74 (5.2), 73 (13.1), 69 (6.9), 64 (7.0), 63 (10.9), 60 (13.5), 57 (22.2), 56 (8.0), 55 (16.1), 51 (11.4), 50 (6.1), 45 (18.7), 44 (8.4), 43 (23.7); LC-MS, *m/z* = 335 [M+1], 337 [M+3]; Anal. Calcd for $C_{18}H_{14}N_4OS$: C, 64.65; H, 4.22; N, 16.75; S, 9.59; Found: C, 64.67; H, 4.21; N, 16.76; S, 9.61.

**3-(Thienyl-2)-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]guinazoline-2-one (4g).** Yield — 89,8%. Mp > 300°C. IR (см$^{-1}$): 3494, 3337, 3091, 3066, 2790, 1652, 1621, 1557, 1532, 1514, 1481, 1398, 1387, 1346, 1309, 1266, 1249, 1225, 1194, 1161, 1110, 1090, 1065, 1047, 999, 983, 957, 933, 865, 854, 799, 774, 750, 732, 699, 683, 621; $^1$H NMR: δ=7.28 (t, 1H, $J$ = 4.4, H-4′), 7.51-7.45 (m, 2H, H-8, 10), 7.83 (t, 1H, $J$ = 7.9, H-9), 7.93 (d, 1H, $J$ = 4.4, H-5′), 8.35-8.33 (m, 2H, H-11, 3'), 13.96 (s, 1H, NH); EI-MS, *m/z* ($I_{rel}$, %) = 312 ($M^{+\bullet}$, 7.3), 205 (5.8), 204 (11.1), 203 (100.0), 171 (6.3), 170 (9.8), 163 (4.0), 161 (30.2), 160 (8.3), 149 (8.7), 146 (7.3), 145 (77.2), 144 (11.2), 143 (25.5), 134 (17.3), 129 (7.3), 119 (5.6), 118 (9.9), 117 (18.3), 116 (6.3), 109 (14.9), 103 (6.8), 102 (21.7), 97 (5.2), 95 (6.6), 90 (16.3), 83 (7.6), 76 (6.1), 75 (7.8), 73 (5.3), 71 (5.0), 70 (5.3), 69 (14.2), 64 (6.3), 63 (5.3), 60 (5.7), 58 (8.2), 57 (11.7), 55 (8.6), 51 (5.2), 45 (14.1), 43 (9.1), 41 (7.8); LC-MS, *m/z* = 313 [M+1], 315[M+3]; Anal. Calcd for $C_{14}H_8N_4OS_2$: C, 53.83; H, 2.58; N, 17.94; S, 20.53; Found: C, 53.81; H, 2.58; N, 17.93; S, 20.53.

**General Procedure for the Synthesis of [(3-R-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio] acetic Acids (5a-f)**

*Method A.* Solution of 0,94 g (10 mmol) chloracetic acid with 0,40 g (10 mmol) of sodium hydroxide in 5 ml of water was added to solution of potassium salt of proper 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-2-on (10 mmol) (**3**) in 20 ml of water, refluxed for 2 hours until the neutral pH. Then 50 ml of water was added to the resulted mixture and filtered. A filtrate was acidified by hydrochloric acid to pH 3. The obtained solid was filtered off and dried.

*Method B.* The proper 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]-quinazoline-2-on (5 mmol) (**4**) and 0,47 g (5 mmol) of chloracetic acid was added to solution of 0,23 g (10 mmol) of metallic sodium in 20 ml of ethanol, refluxed for 2 hours until the neutral pH. Then 50 ml of water was added to the resulted mixture and filtered. A filtrate was acidified by hydrochloric acid to pH 3. The obtained solid was filtered off and dried.

**[(3-Methyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acids (5a).** Yield — 71,9% (method A), 69,4% (method B). Mp — 238-240°C. IR (см$^{-1}$): 2997, 2923, 2843, 2708, 2600, 1713, 1661, 1628, 1605, 1585, 1557, 1505, 1465, 1421, 1388, 1374, 1362, 1329, 1311, 1288, 1265, 1219, 1185, 1156, 1133, 1104, 1045, 955, 879, 774, 687, 630, 610; $^1$H NMR: δ=2.36 (s, 3H, $CH_3$), 4.06 (s, 2H, -S-C$H_2$-), 7.68-7.59 (m, 2H, H-8, 10), 7.93 (t, 1H, $J$=7.9, H-9), 8.41 (d, 1H, $J$ = 7.9, H-11), 12.90 (s, 1H, COOH); $^{13}$C NMR: δ=18.19 ($CH_3$), 34.21 ($SCH_2$), 118.50 (11a), 126.00 (8), 126.76 (10), 128.01 (11), 136.02 (9), 144.09 (11b), 151.93 (3), 154.41 (6), 155.28 (7a), 160.98 (2), 170.04 (COOH); EI-MS, *m/z* ($I_{rel}$, %) = 302 ($M^{+\bullet}$, 2.7), 244 (5.7), 243 (30.6), 219 (4.4), 218 (8.4), 217 (75.1), 216 (25.2), 215 (13.7), 205 (5.2), 204 (5.1), 203 (33.2), 202 (5.0), 198 (5.8), 190 (6.5), 189 (18.2), 188 (20.4), 187 (18.2), 185 (5.1), 177 (6.9), 174 (12.0), 172 (16.1), 171 (61.9), 170 (19.0), 162 (5.3), 161 (17.7), 160 (15.6), 159 (11.3), 157 (5.1), 149 (39.8), 148 (8.7), 146 (8.1), 145 (53.3), 144 (30.4), 143 (90.8), 142 (22.5), 135 (6.2), 134 (20.2), 133 (7.7), 132 (5.8), 131 (5.7), 130 (16.0), 129 (75.9), 128 (5.6), 125 (7.8), 124 (5.0), 123 (21.3), 121 (6.0), 120 (5.2), 119 (15.8), 118 (20.8), 117 (27.6), 116 (30.3), 115 (15.0), 112 (5.1), 111 (15.9), 110 (7.7), 109 (6.8), 107 (7.5), 105 (17.8), 104 (12.9), 103 (14.5), 102 (62.2), 101 (8.5), 99 (7.2), 98 (10.1), 97 (30.2), 96 (10.3), 95 (10.7), 92 (8.4), 91 (12.5), 90 (54.5), 89 (12.6), 88 (6.9), 87 (18.5), 86 (5.3), 85 (65.1), 84 (17.4), 83 (100.0), 82 (17.0), 81 (15.3), 79 (6.7), 77 (18.3), 76 (10.8), 75 (18.8), 74

(9.2), 71 (23.7), 70 (14.7), 69 (38.0), 68 (6.6), 67 (9.1), 65 (7.4), 64 (11.6), 63 (15.9), 62 (5.7), 61 (8.1), 60 (36.9), 59 (5.5), 58 (5.6), 57 (72.4), 56 (32.6), 55 (67.7), 54 (8.2), 53 (5.5), 52 (5.8), 51 (14.6), 50 (10.0), 49 (7.1), 48 (9.8), 47 (24.6), 46 (13.6), 45 (77.0), 43 (74.3), 42 (19.6), 41 (70.6), 40 (14.6); LC-MS, *m/z* = 303 [M+1], 304 [M+2]; Anal. Calcd for $C_{13}H_{10}N_4O_3S$: C, 51.65; H, 3.33; N, 18.53; S, 10.61; Found: C, 51.66; H, 3.34; N, 18.52; S, 10.61.

**[(3-Benzyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acids (5b).** Yield — 85,2% (method A), 80,2% (method B). Mp — 216-218°C. IR ($cm^{-1}$): 3010, 2910, 2681, 2568, 1713, 1661, 1587, 1558, 1506, 1470, 1454, 1434, 1422, 1377, 1341, 1314, 1289, 1262, 1212, 1182, 1153, 1123, 1099, 1072, 1043, 1021, 959, 840, 772, 749, 695, 678, 630, 615; $^1$H NMR: δ=4.04 (s, 2H, $CH_2C_6H_5$), 4.10 (s, 2H, -$SCH_2$), 7.25 (s, 1H, *J*= 7.2, H- 4′), 7.39-7.30 (m, 4H, 2′, 3′, 5′, 6′), 7.67-7.61 (m, 2H, H-8, 10), 7.92 (t, 1H, *J*= 7.9, H-9), 8.41 (d, 1H, *J*=7.9, H-11), 13.92 (s, 1H, COOH); $^{13}$C NMR: δ=34.16 ($SCH_2$), 36.84 ($CH_2$Ph), 118.51 (11a), 126.06 (8), 126.77 (10), 127.24 (4′-Ph), 127.99 (11), 128.80 (3′,5′-Ph), 129.93 (2′,6′-Ph), 136.05 (1′-Ph), 135.93 (9), 144.15 (11b), 151.90 (3), 154.64 (6), 155.86 (7a), 160.45 (2), 170.08 (COOH); EI-MS, *m/z* ($I_{rel}$, %) = 380 (6.1), 379 (20.7), 378 ($M^{+\bullet}$, 80.4), 320 (6.8), 319 (22.9), 244 (5.3), 243 (18.3), 203 (3.7), 219 (5.9), 218 (15.3), 217 (100.0), 216 (53.3), 215 (23.6), 199 (25.8), 198 (81.1), 197 (10.8), 189 (22.3), 188 (26.5), 174 (10.1), 173 (7.2), 172 (29.2), 171 (95.5), 170 (24.6), 166 (5.7), 161 (13.3), 160 (14.2), 159 (6.1), 156 (6.2), 155 (29.7), 149 (6.5), 148 (11.7), 145 (27.7), 144 (20.1), 143 (87.8), 142 (18.8), 134 (9.3), 131 (10.0), 130 (14.2), 129 (57.8), 118 (14.4), 117 (20.5), 116 (28.9), 115 (5.8), 104 (5.4), 103 (13.9), 102 (48.0), 91 (24.1), 90 (37.8), 89 (16.6), 85 (5.6), 83 (6.4), 77 (14.0), 76 (9.9), 75 (10.4), 73 (5.0), 71 (5.0), 69 (7.6), 65 (9.3), 64 (6.9), 63 (9.8), 60 (5.7), 57 (10.9), 56 (11.5), 55 (12.0), 51 (12.4), 50 (6.7), 46 (5.2), 45 (16.4), 43 (9.8), 41 (8.5); LC-MS, *m/z* = 379 [M+1], 381 [M+3]; Anal. Calcd for $C_{19}H_{14}N_4O_3S$: C, 60.31; H, 3.73; N, 14.81; S, 8.47; Found: C, 60.30; H, 3.72; N, 14.81; S, 8.48.

**[(3-Phenyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acids (5c).** Yield — 75,8% (method A), 70,3% (method B). Mp — 270-272°C. IR ($cm^{-1}$): 2865, 2780, 2637, 2534, 2310, 1724, 1637, 1622, 1598, 1564, 1546, 1502, 1482, 1469, 1410, 1387, 1345, 1315, 1286, 1267, 1217, 1180, 1170, 1139, 1106, 1085, 994, 973, 943, 928, 903, 854, 815, 790, 774, 756, 695, 663, 640, 623, 615; $^1$H NMR: δ=4.14 (s, 2H, -$SCH_2$), 7.66-7.58 (m, 3H, H-3′, 4′, 5′), 7.74-7.68 (m, 2H, H-8, 10), 7.98 (t, 1H, *J*= 7.9, H-9), 8.28 (d, 2H, *J*=8.2, H-2′, 6′), 8.49 (d, 1H, *J*= 7.9, H- 11), 12.97 (s, 1H, COOH); EI-MS, *m/z* ($I_{rel}$, %) = 366 (5.9), 365 (26.2), 364 ($M^{+\bullet}$, 8.4), 307 (6.5), 306 (19.1), 305 (75.4), 243 (7.0), 219 (26.7), 218 (63.5), 217 (100.0), 216 (88.8), 215 (64.3), 203 (7.6), 202 (7.8), 190 (8.0), 189 (47.2), 188 (68.3), 187 (6.6), 186 (5.7), 174 (25.8), 172 (38.3), 171 (54.0), 162 (5.5), 161 (17.3), 160 (31.8), 159 (15.9), 155 (6.5), 148 (25.9), 146 (6.2), 145 (39.5), 144 (33.0), 143 (93.1), 142 (36.8), 134 (19.1), 130 (22.6), 129 (80.0), 118 (11.3), 117 (10.8), 116 (30.3), 115 (7.7), 104 (7.4), 103 (39.7), 102 (67.4), 91 (6.6), 90 (56.7), 89 (22.9), 88 (10.2), 77 (16.2), 76 (35.9), 75 (20.7), 64 (11.7), 63 (26.8), 62 (7.3), 56 (15.9), 52 (6.9), 51 (14.7), 50 (12.4), 46 (9.5), 45 (15.0); LC-MS, *m/z* = 307 [M+1], 309 [M+3]; Anal. Calcd for $C_{18}H_{12}N_4O_3S$: C, 59.33; H, 3.32; N, 15.38; S, 8.80; Found: C, 59.33; H, 3.33; N, 15.37; S, 8.81.

**[(3-(4′-Methylphenyl)-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acids (5d).** Yield — 84,9% (method A) та 80,6% (method B). Mp — 234-236°C; IR ($cm^{-1}$): 2850, 2749, 2622, 2515, 1747, 1641, 1605, 1588, 1576, 1561, 1534, 1488, 1470, 1409, 1389, 1347, 1322, 1283, 1268, 1245, 1188, 1157, 1107, 1072, 1019, 993, 968, 939, 897, 857, 832, 772, 762, 715, 685, 647, 627; 1H NMR: δ=2.38 (s, 3H, $CH_3$), 4.10 (s, 2H, -$SCH_2$), 7.37 (d, 2H, *J* = 8.2, H-3′, 5′), 7.71-7.61 (m, 2H, H-8, 10), 7.94 (t, 1H, *J*=7.9, H-9), 8.20 (d, 2H, *J* = 8.2, H-2', 6'), 8.44 (d, 1H, *J*= 7.9, H-11), 12.93 (s, 1H, COOH); EI-MS, *m/z* ($I_{rel}$, %) = 379 (3.0), 320 (7.8), 319 (25.3), 219 (11.8), 218 (28.6), 217 (87.7), 215 (28.6), 204(7.3), 203 (39.6), 189 (35.6), 188 (34.6), 187 (6.7), 177 (8.5), 174 (12.2), 172 (20.0), 171 (100.0), 170 (26.2), 166 (5.8), 161 (18.3), 160 (16.3), 159 (6.5), 149 (8.3), 148 (12.3), 145 (41.3), 144 (20.9), 143 (90.7), 142 (17.0), 134 (14.2), 131 (5.3), 130 (13.0), 129 (52.4), 119 (8.7), 118 (15.2), 117 (18.0), 116 (31.8), 115 (5.4), 103 (14.7), 102 (38.6), 91 (10.2), 90 (35.0), 89 (15.7), 88 (8.7), 77 (13.4), 76 (9.3), 75 (10.7), 73 (7.2), 69 (7.2), 65 (5.7), 64 (7.3), 63 (10.6), 60 (7.7), 58 (7.0), 57 (9.6), 56 (10.9), 55 (7.8), 51 (9.9), 50 (5.0), 45 (18.4), 43 (13.0), 41 (8.4); LC-MS, *m/z* = 321 [M—$CH_2$COOH] $^+$, 379 [M+1], 381 [M+3]; Anal. Calcd for $C_{19}H_{14}N_4O_3S$: C, 60.31; H, 3.73; N, 14.81; S, 8.47; Found: C, 60.32; H, 3.73; N, 14.81; S, 8.49.

**[(3-(4′-Methoxyphenyl)-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acids (5e).** Yield — 77,4% (method A), 70,3% (method B). Mp — 238-242°C. IR ($cm^{-1}$): 2998, 2915, 2835, 2603, 2469, 2310, 2144, 1729, 1632, 1600, 1576, 1559, 1532, 1482, 1455, 1417, 1380, 1337, 1313, 1287, 1270, 1232, 1172, 1156, 1139, 1106, 1069, 1016, 984, 940, 884, 838, 811, 785, 770, 721, 701, 679, 635, 619; $^1$H NMR: δ=3.84 (s, 3H, $OCH_3$), 4.10 (s, 2H, -$SCH_2$), 7.11 (d, 2H, *J*=8.8, H-3′, 5′), 7.72-7.60 (m, 2H, H-10, 8), 7.93 (t, 1H, *J*=7.9, H-9), 8.34 (d, 2H, *J*=8.8, H-2', 6'), 8.44 (d, 1H, *J*=7.9, H-11), 12.89 (s, 1H, COOH); $^{13}$C NMR: δ=34.22 ($SCH_2$), 55.94 ($OCH_3$), 114.45 (3′,5′-Ph), 118.21 (11a), 124.27 (8), 126.00 (10), 126.84 (1′-Ph), 128.04 (11), 131.70 (2′,6′-Ph), 135.90 (9), 144.04 (11b), 148.79 (3), 150.66 (6), 154.63 (7a), 160.20 (2), 162.55 (4′-Ph), 170.08 (COOH); EI-MS, *m/z* ($I_{rel}$, %) = 394 ($M^{+\bullet}$, 5.5), 335 (9.4), 219 (5.3), 218 (13.1), 217 (100.0), 216 (20.0), 215 (11.0), 199 (8.9), 198 (17.3), 189 (13.1), 188 (16.1), 187 (9.0), 185 (5.3), 174 (6.5), 173 (7.5), 172 (25.6), 171 (53.1), 170 (12.8), 161 (5.9), 160 (6.5), 159 (7.7), 155 (13.1), 148 (5.9), 145 (21.8),

144 (11.0), 143 (44.9), 142 (9.7), 134 (13.3), 133 (84.4), 130 (10.6), 129 (38.2), 119 (5.1), 118 (8.7), 117 (7.9), 116 (9.2), 111 (5.4), 104 (5.7), 103 (18.3), 102 (22.4), 98 (7.1), 97 (15.5), 96 (6.2), 95 (11.6), 90 (28.9), 87 (5.0), 85 (10.8), 84 (13.4), 83 (6.4), 82 (8.5), 81 (8.3), 76 (7.2), 73 (15.7), 71 (8.1), 69 (13.8), 67 (7.2), 60 (15.2), 57 (28.6), 56 (11.4), 55 (18.8), 45 (27.2), 43 (19.2), 41 (14.3); LC-MS, *m/z* = 395 [M+1], 397 [M+3]; Anal. Calcd for $C_{19}H_{14}N_4O_4S$: C, 57.86; H, 3.58; N, 14.21; S, 8.13; Found: C, 57.85; H, 3.54; N, 14.20; S, 8.12.

**[(3-(3′,4′-Dimethylphenyl)-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic acids (5f).** Yield — 84,4% (method A), 80,9% (method B). Mp — 226-228°C. IR ($cm^{-1}$): 2955, 2910, 2885, 2846, 2739, 2636, 2517, 1734, 1631, 1581, 1560, 1542, 1503, 1485, 1469, 1411, 1390, 1342, 1320, 1266, 1249, 1183, 1157, 1117, 1080, 1046, 1026, 1016, 990, 957, 898, 888, 870, 834, 786, 773, 757, 710, 686, 640, 610; $^1$H NMR: δ=2.31 (d, 6H, *J*= 4.1, 3,4-($CH_3$)$_2$), 4.11 (s, 2H, S-C$H_2$), 7.33 (d, 1H, *J* = 8.1, H-5′), 7.72-7.64 (m, 2H, H-10, 8), 7.95 (t, 1H, *J*=7.9, H-9), 8.04 (d, 1H, *J*=8.1, H-6'), 8.07 (s, 1H, H-2′), 8.46 (d, 1H, *J* = 7.9, H-11), 12.99 (s, 1H, COOH); EI-MS, *m/z* ($I_{rel}$, %) = 393 (1.0), 333 (10.5), 219 (7.0), 218 (15.6), 217 (100.0), 216 (26.1), 204 (6.7), 203 (45.4), 189 (13.7), 188 (17.2), 174 (6.8), 173 (6.0), 172 (10.7), 171 (48.6), 170 (12.8), 161 (16.9), 160 (8.9), 159 (5.4), 149 (6.7), 148 (5.8), 146 (5.5), 145 (31.0), 144 (12.4), 143 (45.2), 142 (7.5), 134 (14.2), 130 (12.8), 129 (24.7), 119 (6.7), 118 (15.1), 117 (11.6), 116 (34.6), 115 (6.7), 103 (11.4), 102 (19.7), 91 (7.6), 90 (13.8), 77 (8.5), 76 (5.0), 75 (5.1), 73 (5.9), 69 (6.2), 63 (5.4), 60 (6.2), 57 (8.8), 56 (6.8), 55 (8.2), 45 (11.4), 43 (10.4), 41 (8.7); LC-MS, *m/z* = 335 [M—$CH_2COOH$] $^+$, 393 [M+1], 395 [M+3]; Anal. Calcd for $C_{20}H_{16}N_4O_3S$: C, 61.21; H, 4.11; N, 14.28; S, 8.17; Found: C, 61.23; H, 4.13; N, 14.29; S, 8.18.

**General Procedure for the Synthesis of [(3-R-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio) acetic Acids Esters (6a-e)**

*Method A.* The solution 1,22 g (10 mmol) of chloracetic acid ethyl ester in 20 ml of of ethanol was added to the potassium salt of the proper 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]-quinazoline-2-ones (10 mmol) (**3**), refluxed during 2 hours. Then 50 ml of water was added to the resulted mixture and filtered. The obtained solid was dried.

*Method B.* The solution of 0,23 g of metallic sodium (10 mmol) in 20 ml of ethanol was added to the proper 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4]triazino[2,3-*c*]-quinazoline-2-ones (**4**) (10 mmol) and 1,22 g (10 mmol) of chloracetic acid ethyl ester, refluxed for 2 hours. Then 50 ml of water was added to the resulted mixture and filtered. The obtained solid was dried.

*Method C.* 1,0-1,5 ml of the concentrated sulphuric acid was added to the proper [(3-R-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic acid (0,01 Mol) (**6**) dissolved in 10 ml of ethanol and refluxed on the water bath at 80°C during 5-6 hours. Resulted mixture was cooled, poured into the saturated solution of sodium hydrocarbonate. The obtained solid was filtered and dried.

*Method D.* 0,54 ml of thonylchloride (0,075 Mol) and 1 drop of DMF was added to the proper [(3-R-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio] acetic acid (0,005 Mol) (**6**) in 10 ml of ethanol. and refluxed on the water bath at 80°C during 5-6 hours. Resulted mixture was cooled, poured into the saturated solution of sodium hydrocarbonate. The obtained solid was filtered and dried.

**[(3-Methyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acid Ethyl Ester (6a).** Yield — 86,4% (method A), 71,9% (method B), 83,7% (method C), 89,7% (method D). mp — 154-156°C. IR ($cm^{-1}$): 3105, 2985, 2919, 1734, 1663, 1628, 1582, 1555, 1504, 1465, 1431, 1376, 1361, 1338, 1307, 1283, 1262, 1223, 1206, 1190, 1150, 1130, 1104, 1043, 1022, 952, 897, 856, 811, 770, 698, 684, 628, 607; $^1$H NMR: δ=1.22 (t, 3H, $J^1$= 7.1, $J^2$= 1.8, $CH_2C\underline{H}_3$), 2.36 (s, 3H, $CH_3$), 4.21-4.11 (m, 4H, $C\underline{H}_2CH_3$, -S-$CH_2$-), 7.68-7.59 (m, 2H, H-8, 10), 7.93 (t, 1H, $J^3$ = 7.9, $J^4$ = 1.6, H-9), 8.41 (d, 1H, *J* = 7.8, H-11); EI-MS, *m/z* ($I_{rel}$, %) = 331 (2.0), 330 ($M^{+\bullet}$, 7.8), 289 (2.8), 244 (14.4), 243 (56.2), 219 (1.3), 218 (6.9), 217 (28.8), 216 (100.0), 215 (38.8), 204 (1.7), 203 (8.7), 199 (6.1), 189 (1.6), 188 (3.8), 187 (1.3), 186 (2.0), 174 (7.2), 171 (16.2), 170 (20.5), 148 (12.5), 143 (11.1), 142 (7.1), 129 (9.9); LC-MS, *m/z* = 331 [M+1], 333 [M+3]; Anal. Calcd for $C_{15}H_{14}N_4O_3S$: C, 54.54; H, 4.27; N, 16.96; S, 9.71; Found: C, 54.56; H, 4.28; N, 16.96; S, 9.72.

**[(3-Phenyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acid Ethyl Ester (6c).** Yield — 96,4% (method A), 88,5% (method B); 89,7% (method C), 97,3% (method D). Mp — 140-142°C; IR ($cm^{-1}$): 3328, 2974, 2930, 2904, 1727, 1669, 1590, 1566, 1508, 1488, 1463, 1440, 1390, 1368, 1337, 1305, 1272, 1242, 1202, 1180, 1155, 1132, 1083, 1046, 1026, 1000, 990, 938, 879, 865, 849, 813, 785, 775, 756, 697, 689, 650; $^1$H NMR: δ=1.23 (t, 3H, *J*=7.1, $CH_2C\underline{H}_3$), 4.26-4.11 (m, 4H, $C\underline{H}_2CH_3$, -S-$CH_2$-), 7.71-7.51 (m, 5H, H-8, 10, 3′, 4′, 5′), 7.95 (t, 1H, *J* =7.9, H-9), 8.25 (d, 2H, *J* = 8.8, H-2′, 6′), 8.44 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 393 [M+1], 395 [M+3]; Anal. Calcd for $C_{20}H_{16}N_4O_3S$: C, 61.21; H, 4.11; N, 14.28; S, 8.17; Found: C, 61.22; H, 4.13; N, 14.27; S, 8.19.

**[(3-(4′-Methylphenyl)-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic Acid Ethyl Ester (6d).** Yield — 66,6% (method A), 64,3% (method B), 82,3% (method C), 92,3% (method D). Mp — 184-186°C. IR ($cm^{-1}$): 3244, 2984, 2916, 2848, 1735, 1667, 1625, 1610, 1590, 1562, 1547, 1518, 1496, 1485, 1468, 1418, 1383, 1365, 1336, 1310, 1279, 1269, 1241, 1187, 1146, 1134, 1104, 1071, 1020, 986, 952, 940, 903, 863, 834, 787, 773, 756, 722, 711, 702, 681, 640, 625, 614; $^1$H NMR: δ=1,23 (t, 3H, *J*=7.1, $CH_2C\underline{H}_3$), 2.38 (s, 3H, $CH_3$), 4.22-4.12 (m, 4H, -S-C$H_2$-, -C$\underline{H}_2CH_3$), 7.37 (d, 2H, *J*= 8.2, H-3′, 5′), 7.70-7.62 (m, 2H, H-8, 10), 7.94 (t, 1H, *J* = 7.9, H-9), 8.19 (d, 2H, *J* = 8.2, H-2′,

6′), 8.46 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 407 [M+1], 409 [M+3]; EI-MS, *m/z* ($I_{rel}$, %) = 319 (2.7), 318 (5.4), 304 (5.7), 303 (29.2), 289 (1.3), 218 (3.9), 217 (4.3), 216 (14.3), 215 (5.5), 203 (1.4), 188 (1.3), 187 (13.0), 186 (100.0), 185 (1.8), 159 (11.0), 143 (18.5), 117 (13.5), 116 (14.4), 90 (5.3). Anal. Calcd for $C_{21}H_{18}N_4O_3S$: C, 62.06; H, 4.46; N, 13.78; S, 7.89; Found: C, 62.04; H, 4.44; N, 13.78; S, 7.91.

**[(3-(4′-Methoxylphenyl)-2-oxo-2*H*-[1,2,4]triazino [2,3-*c*]quinazoline-6-yl)thio]acetic Acid Ethyl Ester (6e).** Yield — 80,6% (method A), 74,8% (method B), 84,8% (method C), 94,8% (method D). Mp — 144-146°C; IR ($cm^{-1}$): 3108, 3076, 3010, 2967, 2930, 2839, 1737, 1663, 1600, 1586, 1550, 1545, 1495, 1468, 1419, 1371, 1340, 1317, 1302, 1284, 1268, 1253, 1240, 1196, 1175, 1157, 1136, 1117, 1105, 1073, 1031, 989, 941, 895, 882, 865, 837, 809, 767, 722, 704, 686, 643, 623; $^1$H NMR: δ=1.23 (t, 3H, *J*= 7.1, $CH_2C\underline{H}_3$), 3.84 (s, 3H, $OCH_3$), 4.23-4.11 (m, 4H, $C\underline{H}_2CH_3$, -S-$CH_2$-), 7.11 (d, 2H, *J*= 8.8, H-3′, 5′), 7.70-7.60 (m, 2H, H-8, 10), 7.94 (t, 1H, *J* = 7.9, H-9), 8.33 (d, 2H, *J* = 8.8, H-2′, 6′), 8.41 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 423 [M+1], 425 [M+3]. Anal. Calcd for $C_{21}H_{18}N_4O_4S$: C, 59.71; H, 4.29; N, 13.26; S, 7.59; Found: C, 59.73; H, 4.30; N, 13.25; S, 7.57.

**General Procedure for the Synthesis of [(3-R-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio] acetic Acid Amides (7a-e).** 0,93 g (10 mmol) of chloracetamide was added to the suspension of potassium salt of the proper 3-R-6-thio-6,7-dihydro-2*H*-[1,2,4] triazino[2,3-*c*]-quinazoline-2-on (**3**) (10 mmol) in 20 ml of propanol-2 and refluxed during 2 hours. Resulted mixture was cooled, solid was filtered and dried.

**[(3-Methyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic acid amide (7a).** Yield — 53,3%. Mp — 260-262°C. IR ($см^{-1}$): 3294, 3147, 2782, 1687, 1657, 1628, 1603, 1581, 1556, 1504, 1467, 1427, 1403, 1388, 1363, 1336, 1317, 1287, 1264, 1233, 1208, 1157, 1137, 1106, 1045, 956, 897, 771, 682, 673, 631, 605; $^1$H NMR: δ=2.35 (s, 3H, $CH_3$), 3.96 (s, 2H, -S-$CH_2$-), 7.27 (s, 1H, $NH_2$), 7.76-7.58 (m, 3H, H-8, 10, $NH_2$), 7.93 (t, 1H, *J*= 7.9, H-9), 8.41 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 260, 302 [M+1], 304 [M+3]; Anal. Calcd for $C_{13}H_{11}N_5O_2S$: C, 51.82; H, 3.68; N, 23.24; S, 10.64; Found: C, 51.84; H, 3.66; N, 23.25; S, 10.64.

**[(3-Phenyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic acid amide (7c).** Yield — 78,4%. Mp — 240-242°C; IR ($см^{-1}$): 3397, 3272, 3200, 1669, 1659. 1619, 1586, 1562, 1550, 1503, 1486, 1468, 1443, 1409, 1388, 1372, 1338, 1311, 1284, 1267, 1238, 1182, 1160, 1137, 1104, 1080, 1030, 1021, 1002, 990, 940, 903, 883, 813, 784, 772, 755, 690, 653, 633, 613; $^1$H NMR: δ=4.00 (s, 2H, -S-$CH_2$-), 7.30 (s, 1H, $NH_2$), 7.78-7.52 (m, 6H, H-8, 10, 3′, 4′, 5′, $NH_2$), 7.97 (t, 1H, *J* =7.9, H-9), 8.27 (d, 2H, *J* = 8.8, H-2′, 6′), 8.47 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 364 [M+1], 366[M+3]; Anal. Calcd for $C_{18}H_{13}N_5O_2S$: C, 59.49; H, 3.61; N, 19.27; S, 8.82; Found: C, 59.48; H, 3.64; N, 19.28; S, 8.84.

**[(3-(4′-Methylphenyl)-2-oxo-2*H*-[1,2,4]triazino [2,3-*c*]quinazoline-6-yl)thio]acetic acid amide (7d).** Yield — 69,3%. Mp — 264-267°C; IR ($cm^{-1}$): 3434, 3314, 1682, 1664, 1589, 1561, 1543, 1496, 1469, 1400, 1367, 1341, 1311, 1272, 1240, 1190, 1161, 1135, 1108, 1075, 1021, 991, 940, 885, 833, 784, 772, 707, 686, 643, 629; $^1$H NMR: δ=2.39 (s, 3H, $CH_3$), 4.00 (s, 2H, -S-$CH_2$-), 7.30 (s, 1H, $NH_2$), 7.39 (d, 2H, *J*= 8.2, H-3′, 5′), 7.78-7.64 (m, 3H, H-8, 10, $NH_2$), 7.96 (t, 1H, *J* = 7.9, H-9), 8.22 (d, 2H, *J* = 8.2, H-2′, 6′), 8.46 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 378 [M+1], 380[M+3]; Anal. Calcd for $C_{19}H_{15}N_5O_2S$: C, 60.47; H, 4.01; N, 18.56; S, 8.50; Found: C, 60.46; H, 4.03; N, 18.54; S, 8.52.

**[(3-(4′-Methoxylphenyl)-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio]acetic acid amide (7e).** Yield — 76,9%. Mp — 224-226°C. IR ($cm^{-1}$): 3200, 1657, 1601, 1590, 1562, 1538, 1495, 1476, 1467, 1435, 1420, 1373, 1340, 1319, 1303, 1256, 1175, 1138, 1118, 1108, 1075, 1021, 987, 942, 841, 771, 686, 639, 623; $^1$H NMR: δ=3.84 (s, 3H, $OCH_3$), 4.00 (s, 2H, -S-$CH_2$-), 7.17-7.04 (m, 3H, H-3′, 5′, $NH_2$), 7.29 (s, 1H, $NH_2$), 7.76-7.60 (m, 2H, H-8, 10), 7.94 (t, 1H, *J* = 7.9, H-9), 8.35 (d, 2H, *J* = 8.8, H-2′, 6′), 8.45 (d, 1H, *J* = 7.9, H-11); LC-MS, *m/z* = 320, 321, 394 [M+1]; Anal. Calcd for $C_{19}H_{15}N_5O_3S$: C, 58.01; H, 3.84; N, 17.80; S, 8.15; Found: C, 58.03; H, 3.85; N, 17.81; S, 8.16.

**Crystal structure determination of [(3-Methyl-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-6-yl)thio] acetic Acid (5a).** Crystals of **5a** are triclinic, $C_{13}H_{10}N_4O_3S$, at 20°C *a* = 7.4911(10), *b* = 9.4189(15), *c* = 10.4215(15) A°, α = 65.065(15)°, β = 87.152(12)°, γ = 79.555(13)°, V = 655.43(17) $A^{°3}$, $M_r$ = 302.31, Z = 2, space group P1, $d_{sub}$ = 1,532 $g/cm^3$, μ (MoKα) = 0,264 $mm^{-1}$, F(000) = 312. Data collection was performed on a "Xcalibur 3" diffractometer (MoKα radiation, ω scans, CCD detector). It was collected 8102 reflections ($2\theta_{max}$ = 60°, 4101 independent reflections, $R_{int}$ = 0.027). Structure was solved by direct methods and refined against $F^2$ by full-matrix least squares procedure using SHELX-97 program package [24]. All non-hydrogen atoms were refined in anisotropic approximation. Hydrogen atom positions were initially located from difference electron density maps and refined isotropically. Final refinement was converged at $wR_2$ = 0.047 for all 3779 reflections ($R_1$ = 0.033 for 1798 reflections with F>4σ (F), S = 0.68).

Atom coordinates and crystallographic parameters have been deposited to the Cambridge Crystallographic Data Centre (CCDC 766559). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

## Biological Activity Evaluation Methods

The investigation of antimicrobial and antifungal activity of thiones **3-7** was carried out with the stiff plate agar diffusion method against *Escherichia coli, Staphylococcus aureus, Mycobacterium luteum, Can-*

*dida tenuis* and *Aspergillus niger*. The amount of microbial cells was 109 c.f.u./ml. Incubation period of bacteria was 24 hours at 35°C, yeast — 48-72 hours at 28-30°C. Antibiotics vancomicin, oxacillin, nistatin were used as standards. The bacterial cultures, standards and obtained substances in 0,1% and 0,5% concentration were streaked across grooves, and then allowed to diffuse in the agar nutrient plate. The antimicrobial effect and degree of activity of the tested compounds were evaluated by measuring the zone diameters and the results were compared with well known drugs. Repetition of experiment was three-multiple.

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