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SYNTHESIS AND ANTITUMOR PROPERTIES OF 3-(2,2-DIMETHYLTETRAHYDRO-2H-PYRAN-4-YL)SPIRO[BENZO[h]QUINAZOLINE-5,1'-CYCLOHEPTAN]-4(6H)-ONES

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Regioselective addition of benzylmagnesium chloride to ethyl 2-cyano-2-cycloheptylidene-acetate yielded 2-(1-benzylcycloheptyl)-2-cyanoacetate, cyclization of which was used to synthesize ethyl-4'-amino-1'H-spiro[cycloheptane-1,2'-naphthalene]-3'-carboxylate (aminoester). By reacting the amino ester with 4-isothiocyanato-2,2-dimethyltetrahydro-2H-pyran the corresponding thioreido derivative was obtained, which without isolation from the reaction medium, was subjected to cyclization, leading to the synthesis of 3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-thioxo-2,3-dihydro-1H-spiro[benzo[h]-quinazoline-5,1'-cycloheptan]-4(6H)-one. In the presence of bases, thioxoderivative reacted with halides, leading to the formation of 2-sulfanyl-substituted 3-(2,2-dimethyl-tetrahydro-2H-pyran-4-yl)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-ones. The antitumor and antibacterial activity of synthesized compounds was studed.

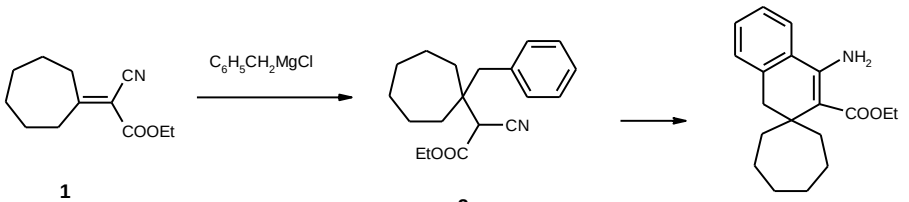
Figs. 2, tables 2, references 18.

Benzo[h]quinazoline compounds have antimicrobial [1-3], antitumor [4,5], antidepressant [6], serotonin antagonist [7], antiphlogistic [8], antiviral [9], antitubercular [10] properties. Our previous work on the synthesis of spirocondensed benzo[h]quinazolines, containing cyclopentane cyclohexane or cycloheptan rings at C5 position, has shown that they possess antimonoaminoxidaze, antitumor, anticonvulsant properties [11-15]. There is a report on the synthesis of benzo[h]quinazolines containing tetrahydropyranic substituents in the 3rd position that act directly on muscarinic M1 receptors and can be used in the treatment of schizophrenia, sleep disorders and Alzheimer's disease [16]. of schizophrenia and sleep disorders

We set ourselves the goal of developing methods for the synthesis of 3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-thioxo-2,3-dihydro-1H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one, which will make it possible

to obtain the corresponding 2-sulfanyl-substituted derivatives and to study some of the biological properties of the synthesized compounds. To carry out the planned work, it was necessary to develop a method for the synthesis of the corresponding β-aminoester of the dihydronaphthalene series and a method for the synthesis of the isothiocyanate of the tetrahydropyran series.

Ethyl 2-cyano-2-cycloheptylideneacetate (**1**) was put into reaction with benzylmagnesium chloride and, as a result of regioselective addition, ethyl 2-(1-benzylcycloheptyl)-2-cyanoacetate (**2**) was obtained. The latter was cyclized in the presence of sulfuric acid leading to ethyl 4'-amino-1'H-spiro[cycloheptane-1,2'-naphthalene]-3'-carboxylate (**3**) (aminoester **3**).



1 **2** **3**

In the IR spectrum of compound **3** there is characteristic absorption of the aromatic ring, C=C double bond and aminogroup in the regions of 1600, 1632 and 3305 cm^{-1}. However, there is no absorption in the spectrum, characteristic of the ester group at 1700-1750 cm^{-1}. An explanation of this phenomenon is given by the X-ray structural analysis, according to which the molecules of compound 3 contain both intramolecular and intermolecular hydrogen bonds. All diffraction measurements were carried out at room temperature on an Enraf-Nonius Cad-4 automated diffractometer (graphite monochromator, Mo-Kα radiation, θ/2θ-scan). The monoclinic unit cell parameters were measured and refined using the diffraction angles of 24 reflections ($14<\theta<16$). The structure was determined by direct method and refined using the software package SHELXTL [17]. All non-hydrogen atoms were refined anisotropically by full-matrix least squares method. The coordinates of all hydrogen atoms were determined from difference Fourier map and refined freely. Crystallographic and experimental data are listed in Table 1. The full crystallographic data in CIF format available free of charge via internet at: http://www.ccdc.cam.ac.uk/products/csd/request/, deposition number: CCDC 1860664.

Table 1

Crystallographic and experimental data

Crystal Data	
Formula	$C_{19}H_{25}NO_2$
Formula Weight	299.40
Crystal System	monoclinic
Space group	$P2_1/n$
a, b, c [Å]	15.060(3), 7.3505(15), 16.331(3)
α, β, γ [deg.]	90, 114.79(3), 90
V [$Å^3$]	1641.2(7)
Z	4
D(calc) [g/cm^3]	1.212
μ(MoKα) [mm^{-1}], T_{min}, T_{max}	0.078
F(000)	648
Crystal Size [mm]	0.42×0.36×0.30
Data Collection	
Temperature (K)	293
Radiation [Å]	MoKα 0.71073
θ_{min}, θ_{max} [Deg]	1.5, 30.0
Dataset	$0 \leq h \leq 21$; $0 \leq k \leq 10$; $-22 \leq l \leq 22$
Tot., Uniq. Data, R(int)	4937, 4772, 0.058
Observed data [I > 2.0 σ(I)]	2819
Refinement	
Nref, Npar	4772, 299
R, wR2, S	0.0656, 0.2271, 1.03

The atomic structure of the molecule is shown in Fig. 1. The conformational analysis of cyclic fragments has shown that the atoms of phenyl ring are in the plane (maximum deviation does not exceed 0.0070 (2) Å), the cyclohexene ring has a half-chair conformation, the C7, C9, C15 and C17 atoms are in the plane while C6 and the C16 atoms are deviated from the plane accordingly -0.4743 (2) Å and -0.9142 (2) Å, the cycloheptanone ring has twist-boat conformation C17, C18, C20 and C21 atoms are in the plane, and C16, C19 and C22 atoms are shifted from the plane on 1.0679(2)Å Å, -0.6535 (2) Å and 1.1495 (2) Å, respectively. There is an intramolecular hydrogen bond between the N8-H8A ..... O5 atoms, the donor-acceptor distance is 2.572 (4) Å (Fig.1). Considering the 3D packing of molecules in the crystal structure, it has been found that there is also an intermolecular hydrogen bond between the N8-H8B ..... $O5^i$ atoms, the donor-acceptor distance is 2.959 (3) Å (Fig. 2). By contacting the molecules, this hydrogen bond generates an infinite chain parallel to the [0 1 0] crystallographic direction (Fig. 2), and the interaction between the chains may be mainly described by the Van der Waals forces.

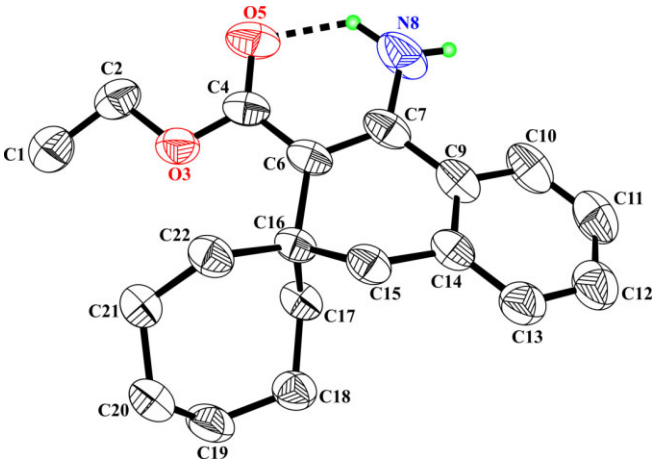


Fig 1. Atomic structure of the molecule $C_{19}H_{25}NO_2$, the ellipsoids of thermal vibrations are drawn on 50% probability level. The intramolecular hydrogen bond is shown by dashed line, for the simplicity of the Figure, the hydrogen atoms not involved in bonding are not drawn.

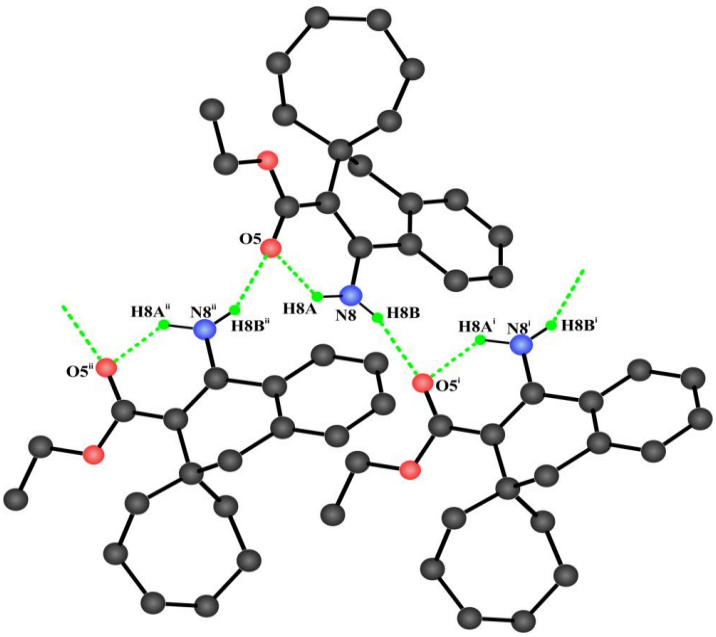
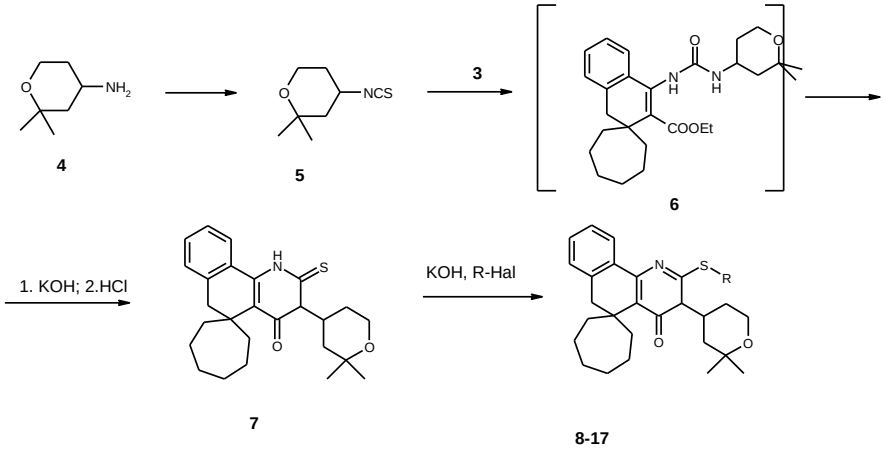


Fig. 2. The infinite chain formed by molecules $C_{19}H_{25}NO_2$ via hydrogen bonds, shown by dashed lines.

Based on 2,2-dimethyltetrahydro-2H-pyran-4-amine (**4**), a method for the synthesis of 4-isothiocyanato-2,2-dimethyltetrahydro-2H-pyran (**5**) has been developed. By reacting the aminoester **3** with isothiocyanate **5** corresponding thioreido derivative **6** was obtained, which, without isolation from the reaction medium, was subjected to cyclization, leading to the synthesis of 3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-2-thioxo-2,3-dihydro-1H-spiro[benzo[h]quinazoline-5,1'-cyclo-heptan]-4(6H)-one (**7**). The latter in the presence of potassium hydroxide reacted with halides of various structures resulting in 2-sulfanyl-

substituted 3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-ones (**8-16**).



4 **5** **6** **7** **8-17**

R=CH_3 (**8**), C_2H_5 (**9**), C_3H_7 (**10**), i-C_3H_7 (**11**), $CH_2CH_2CH(CH_3)_2$ (**12**), $CH_2CH{=}CH_2$ (**13**), $CH_2C(CH)_3{=}CH_2$ (**14**),$CH_2C_6H_5$ (**15**), 2-$CH_3C_6H_4CH_2$ (**16**)

The antitumor properties of compounds on sarcoma 180 model were studied [6]. In chemotherapeutic experiments compounds **7, 9, 11** showed average therapeutic action against sarcoma 180 (inhibition of tumor growth by 40-56%). Weak activity showed compounds **8, 12, 15, 16,** which in a dose of 155-170 *mg*/*kg* inhibited the growth of sarcoma 180 in the range of 32-38%. Compounds **13** and **14** did not exhibit extreme antitumor activity.

The antibacterial activity of synthesized compounds was studied according to the method of diffusion in agar at microbial loading of 20 million Microbial cells per 1 *mL* of media. Gram-positive cocci (Staph. aureus 209P, and 1 and gram-negative bacteria (Sh. dysenteriae 6858, and E. coli O55) were used as the test-objects and Furazolidone was used as a control (Table 2).

Table 2

The antibacterial activity of synthesized compounds

Comp. №	Zone of microbial absence (d, *mm*)			
	Staphylococcus aureus		Sh. Flexneri 6858	E.coli 0-55
	209p	1		
8	0	0	10	0
9	10	10	10	10
10	11	10	10	10
11	10	10	10	10
12	10	10	11	15
13	10	10	13	11
Furazolidone	25	24	24	24,5

Experimental Section

The IR spectra were recorded on a Thermo Nicolet Nexus FT-IR spectrometer from samples dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury-300 instrument from solutions in DMSO-*d*6–CCl_4 (1 : 3); the chemical shifts were measured relative to tetramethylsilane or hexamethyldisiloxane as internal standard. Silufol plates were used for analytical TLC; spots were visualized by treatment with iodine vapor.

Ethyl 2-(1-benzylcycloheptyl)-2-cyanoacetate (2). The solution of 41.4 *g* (0.2 *mol)* of ethyl-2-cyano-2-cycloheptylideneacetate **(1)** in 100 *ml* of absolute ether was added dropwise to the ethereal solution of the Grignard reagent, which had been obtained from 7.6 *g* (0.3 *mol*) of magnesium shavings and 38 *g* (0.3 *mo*l) of benzylchloride in 500 *ml* of absolute diethyl ether. The reaction mixture was mixed at room temperature for 5 *h*, then 125 *ml* of 18% HCl was added while maintaining the temperature at 18-22°C and mixed at room temperature until the complex was decomposed completely. The organic layer was separated, washed with water and dried with sodium sulfate. After distilling off the solvent, the residue was distilled in vacuo. Yield 50.2 *g* (83%) of **2**, bp 205–206°C/5 *mm*, R_f 0.44 (benzene–hexane, 5:2). IR spectrum, ν, cm^{-1}: 1580, 1602 (C=C arom); 1731 (C=O); 2241 (CN). ^{1}H NMR spectrum, δ, ppm: 1.32 (t, 3H, J=7.12, O-CH_2-$\underline{CH_3}$), 1.35-1.56 (m, 8H, cycloheptane), 1.60-1.75 (m, 3H, cycloheptane), 1.85-1.96 (m, 1H, cycloheptane), 2.75 (d, 1H, J=13.57, CH_a-Ph), 2.87 (d, 1H, J=13.57, CH_b-Ph), 3.42 (s, 1H, CH-C≡N), 4.21 (q, 2H, J=7.12, O-$\underline{CH_2}$-CH_3), 7.18-7.31 (m, 5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 13.49 (O-CH_2-$\underline{CH_3}$), 22.38 (CH_2 cycloheptane), 22.43 (CH_2 cycloheptane), 29.94 (CH_2 cycloheptane), 29.96 (CH_2 cycloheptane), 35.04 (CH_2 cycloheptane), 35.28 (CH_2 cycloheptane), 43.81 (C cycloheptane), 43.88 ($\underline{CH_2}$-Ph), 45.84 ($\underline{CH}$-C≡N), 61.44 (O-$\underline{CH_2}$-CH_3), 115.54 (C≡N), 126.18 (CH Ar), 127.57 (2×CH Ar), 130.08 (2×CH Ar), 135.88 (C Ar), 164.79 (C=O). Found, %: C 76.11; H 8.59; N 4.53.$C_{19}H_{25}NO_2$. Calculated, %: C 76.22; H 8.42; N 4.68.

Ethyl 4'-amino-1'H-spiro[cycloheptane-1,2'-naphthalene]-3'-carboxylate (3). 30.2 *g* (0.1 *mol*) of ethyl 2-(1-benzylcycloheptyl)-2-cyanoacetate **(2)** was inserted into the reaction flask and 60 *ml* of concentrated sulfuric acid was added by mixing at 5-10 °C. The mixing at this temperature lasted for 7 *h*, then it was neutralized by NH_4OH and extracted by ether. The extract was washed with water and dried with $MgSO_4$. Then the solvent was removed and the residue was recrystallized from 80% ethanol. Yield 19.3 *g* (64 %) of **3**, mp 57-58°C. R_f 0.67 (ethylacetate–benzene, 1□1). IR spectrum, ν, cm^{-1}: 1600 (C=C arom); 1632 (C=C); 3305.8 (NH_2). ^{1}H NMR spectrum, δ, ppm. 1.25-1.68 (m, 10H, cycloheptane), 1.33 (t, 3H, J=7.14, O-CH_2-$\underline{CH_3}$), 2.03-2.16 (m, 2H, cycloheptane), 2.74 (s, 2H, C1'H_2), 4.18 (q, 2H, J=7.14, O-$\underline{CH_2}$-CH_3), 6.94 (br.s, 2H, NH_2), 7.08-7.16 (m, 1H, CH Ar), 7.18-7.27 (m, 2H, 2×CH Ar), 7.52-7.60 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 14.15 (O-CH_2-$\underline{CH_3}$), 24.20 (2×CH_2, cycloheptane), 29.26 (2×CH_2, cycloheptane), 37.20 (2×CH_2, cycloheptane), 39.00 (C, cycloheptane), 41.40

(C1'H_2), 57.77 (O-$\underline{CH_2}$-CH_3), 104.14 (C3'), 122.49 (CH Ar), 125.69 (CH Ar), 127.07 (CH Ar), 128.46 (CH Ar),130.72 (C Ar), 136.39 (C Ar), 149.74 (C4'), 169.50 (C=O). Found, %: C 76.11; H 8.59; N 4.53. $C_{19}H_{25}NO_2$. Calculated, %: C 76.22; H 8.42; N 4.68.

4-Isothiocyanato-2,2-dimethyltetrahydro-2H-pyran (5). A mixture of 12.9 g (0.1 *mol*) of 2,2-dimethyltetrahydro-2H-pyran-4-amine, 10.1 g (0.1 *mol*) of Rt_3N and 100 *ml* of $CHCl_3$ was placed into the reaction flask. At 10-15 °C, were added 7.6 g (0.1 *mol*) of CS_2, then successively 10.1 g (0.1 *mol*) of Rt_3N and 7.85 g (0.1 *mol*) of acetyl chloride. The reaction mixture was stirred at room temperature for 5 *h*, washed with water and dried with Na_2SO_4. After distilling off the solvent, the residue was distilled in vacuo.Yield 10.0 *g* (58%) of **5**, bp 105–106 °C/5mm. IR spectrum, ν, cm^{-1}: 1194 (C-O-C); 2094 (N=C=S). ^{1}H NMR spectrum, δ, ppm: 1.17 (s, 3H, C2-$(CH_3)_a$), 1.21 (s, 3H, C2-$(CH_3)_b$), 1.50-1.72 (m, 2H, C3H_a, C5H_a), 1.91-2.04 (m, 2H, C3H_b, C5H_b), 3.56 (ddd, 1H, J=2.61, 11.27, 12.37, C6H_a), 3.70 (ddd, 1H, J=2.87, 5.01, 12.37, C6H_b), 4.05 (tt, 1H, J=4.22, 10.83, C4H). ^{13}C NMR spectrum, δ_C, ppm: 22.37 (C2-$(CH_3)_a$), 29.89 (C2-$(CH_3)_b$), 32.94 (C5H_2), 42.88 (C3H_2), 50.42 (C4H), 58.34 (C6H_2), 70.87 (C2), 130.86 (N=C=S). Found, %: 56.23; H 7.45; N 8.08; S 18.57. $C_8H_{13}NOS$. Calculated, %: C 56.11; H 7.65; N 8.18; S 18.72.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-thioxo-2,3-dihydro-1H-spiro[benzo[h]- quinazoline-5,1'-cycloheptan]-4(6H)-one (7). A mixture of 15.0 g (0.05 *mol*) of ethyl 4'-amino-1'H-spiro[cycloheptane-1,2'-naphthalene]-3' carboxylate (**3**), 100 *ml* of ethanol, 8.51g (0.05 *mol*) of 4-isothiocyanato-2,2-dimethyltetrahydro-2H-pyran was placed into a 250 *ml* round-bottomed flask. The reaction mixture was refluxed for 20 *h*, a solution of 5.6 *g* (0.1 *mol*) of KOH in 50 ml of H_2O was added and the mixture was boiled for an additional 3 h. After cooling, the mixture was acidified with a solution of 10% hydrochloric acid. The precipitated crystals were filtered, washed with water, hexane, and recrystallized from ethanol. Yield 13.0 *g* (61%) of **7,** mp 238-239°C, R_f 0.60 (ethylacetate-benzene–hexane, 1□5□5). IR spectrum, ν, cm^{-1}: 1615 (C=C arom); 1673 (C=O); 3169 (NH). ^{1}H NMR spectrum, δ, ppm: 1.23 (s, 3H, C2'-$(CH_3)_a$), 1.23-1.32 (m, 2H, CH_2, cycloheptane), 1.32 (c, 3H, C2'-$(CH_3)_b$), 1.40-1.86 (m, 10H, 5×CH_2, cycloheptane), 2.14-2.32 (m, 2H, C3'H_a, C5'H_a), 2.51-2.60 (m, 1H, C3'H_b), 2.67-2.84 (m, 1H, C5'H_b), 2.84 (s, 2H, C_6H_2), 3.63-3.81 (m, 2H, C6'H_2), 6.05-6.18 (m, 1H, C4'H), 7.17-7.40 (m, 3H, 3×CH Ar), 7.90-7.96 (m, 1H, CH Ar), 11.88 (br, 1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 21.51 (C2'-$\underline{(CH_3)_a}$), 23.71 (CH_2, cycloheptane), 23.77 (CH_2, cycloheptane), 27.29 (C5'H_2), 29.20 (CH_2, cycloheptane), 29.30 (CH_2, cycloheptane), 31.26 (C2'-$\underline{(CH_3)_b}$), 34.95 (CH_2, cycloheptane), 35.45 (CH_2, cycloheptane), 37.16 (C3'H_2), 39.56 (C5), 40.11 (C_6H_2), 55.58 (C4'H), 60.55 (C6'H_2), 72.05 (C2'), 120.61 ($C4_a$), 124.46 (CH Ar), 125.17 (C Ar), 126.04 (CH Ar), 127.63 (CH Ar), 130.35 (CH Ar), 136.38 (C Ar), 141.77 ($C10_b$), 159.75 (C=O), 176.26 (C=S). Found, %: C 70.88; H 7.75; N 6.78; S 7.44. $C_{25}H_{32}N_2O_2S$. Calculated, %: C 70.72; H 7.60; N 6.60; S 7.55.

2-Alkylthio-3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-ones (8-16) (General method). A mixture of 2.12 *g* (0.005 *mol*) of **7**, 0.4 g (0.007 *mol*) of KOH and 30 *ml* of absolute ethanol was placed into a single-necked round-bottomed flask and boiled for 30 *min*. Then 0.07 *mol* of halogenide was added and boiling was continued for 12 *h*. The reaction mixture was cooled and 20 *ml* of water was added. The precipitate was filtered off and recrystallized from ethanol.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-(methylthio)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one (8), (R=CH_3): Yield 1.85 g (84%), mp 197-198^{o}C, R_f 0.62 (ethylacetate-benzene–hexane, 1:5:7): IR spectrum, ν, cm^{-1}. 1600 (C=C arom); 1666 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.26 (s, 3H, C2'-$(CH_3)_a$), 1.30 (c, 3H, C2'-$(CH_3)_b$), 1.31-1.41 (m, 2H, CH_2, cycloheptane), 1.45-1.87 (m, 10H, 5×CH_2, cycloheptane), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.67 (s, 3H, S-CH_3), 2.68-2.79 (m, 1H, C3'H_b), 2.86 (s, 2H, C6H_2), 2.87-3.02 (m, 1H, C5'H_b), 3.60-3.73 (m, 1H, C6'H_a), 3.76-3.85 (m, 1H, C6'H_b), 4.44-4.66 (m, 1H, C4'H), 7.12-7.17 (m, 1H, CH Ar), 7.20-7.32 (m, 2H, 2×CH Ar), 7.98-8.04 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm:14.82 (S-CH_3), 21.23 (C2'-$\underline{(CH_3)_a}$), 23.78 (CH_2, cycloheptane), 23.86 (CH_2, cycloheptane), 27.57 (C5'H_2), 29.38 (CH_2, cycloheptane), 29.49 (CH_2, cycloheptane), 31.06 (C2'-$\underline{(CH_3)_b}$), 35.24 (CH_2, cycloheptane), 35.75 (CH_2, cycloheptane), 37.56 (C3'H_2), 39.79 (C5), 40.03 (C6H_2), 54.82 (C4'H), 60.26 (C6'H_2), 71.73 (C2'), 124.08 (C Ar), 124.59 (CH Ar), 125.89 (CH Ar), 127.19 (CH Ar), 129.46 (CH Ar), 131.88 ($C4_a$), 136.22 (C Ar), 149.77 ($C10_b$), 157.92 (C2), 161.07 (C=O). Found, %: C 71.33; H 7.96; N 6.23; S 7.15. $C_{26}H_{34}N_2O_2S$. Calculated, %: C 71.19; H 7.81; N 6.39; S 7.31.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-(ethylthio)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one (9), (R=C_2H_5):Yield 1.8 g (79%), mp 164–165^{o}C, R_f=0.63 (ethylacetate-benzene–hexane, 1:5:7):IR spectrum, ν, cm^{-1}. 1603 (C=C arom); 1661 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.26 (s, 3H, C2'-$(CH_3)_a$), 1.30 (s, 3H, C2'-$(CH_3)_b$), 1.31-1.42 (m, 2H, CH_2, cycloheptane), 1.45-1.88 (m, 10H, 5×CH_2, cycloheptane), 1.49 (t, 3H, J=7.34, S-CH_2-$\underline{CH_3}$), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.68-2.80 (m, 1H, C3'H_b), 2.86 (s, 2H, C6H_2), 2.87-3.02 (m, 1H, C5'H_b), 3.29 (q, 2H, J=7.34, S-$\underline{CH_2}$-CH_3), 3.61-3.74 (m, 1H, C6'H_a), 3.76-3.85 (m, 1H, C6'H_b), 4.45-4.65 (m, 1H, C4'H), 7.12-7.17 (m, 1H, CH Ar), 7.20-7.32 (m, 2H, 2×CH Ar), 7.93-7.98 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 13.56 (S-CH_2-$\underline{CH_3}$), 21.25 (C2'-$\underline{(CH_3)_a}$), 23.77 (CH_2, cycloheptane), 23.86 (CH_2, cycloheptane), 26.25 (S-$\underline{CH_2}$-CH_3), 27.53 (C5'H_2), 29.38 (CH_2, cycloheptane), 29.49 (CH_2, cycloheptane), 31.06 (C2'-$\underline{(CH_3)_b}$), 35.26 (CH_2, cycloheptane), 35.76 (CH_2, cycloheptane), 37.53 (C3'H_2), 39.81 (C5), 40.06 (C_6H_2), 54.70 (C4'H), 60.24 (C6'H_2), 71.73 (C2'), 124.16 (C Ar), 124.39 (CH Ar), 125.93 (CH Ar), 127.24 (CH Ar), 129.45 (CH Ar), 131.91 ($C4_a$), 136.25 (C Ar), 149.82 ($C10_b$), 157.47 (C2), 161.13 (C=O). Found, %: C 71.79; H 8.19; N 6.03; S 7.23. $C_{27}H_{36}N_2O_2S$. Calculated, %: C 71.64; H 8.02; N 6.19; S 7.08.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-(propylthio)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one (10), (R=C_3H_7): Yield 1.9 g (81%), mp 144–145°C, R_f 0.66 (ethylacetate-benzene–hexane, 1:5:7): IR spectrum, ν, cm^{-1}. 1603 (C=C arom); 1659 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.12 (t, 3H, J=7.36, S-CH_2-CH_2-$\underline{CH_3}$), 1.26 (s, 3H, C2'-$(CH_3)_a$), 1.30 (s, 3H, C2'-$(CH_3)_b$), 1.31-1.41 (m, 2H, CH_2, cycloheptane), 1.45-1.87 (m, 10H, 5×CH_2, cycloheptane), 1.79-1.93 (m, 2H, S-CH_2-$\underline{CH_2}$-CH_3), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.68-2.80 (m, 1H, C3'H_b), 2.86 (s, 2H, C6H_2), 2.87-3.02 (m, 1H, C5'H_b), 3.17-3.34 (m, 2H, S-$\underline{CH_2}$-CH_2-CH_3), 3.61-3.74 (m, 1H, C6'H_a), 3.76-3.85 (m, 1H, C6'H_b), 4.45-4.65 (m, 1H, C4'H), 7.12-7.17 (m, 1H, CH Ar), 7.20-7.32 (m, 2H, 2×CH Ar), 7.91-7.97 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 13.07 (S-CH_2-CH_2-$\underline{CH_3}$),21.26 (C2'-$\underline{(CH_3)_a}$), 21.61 (S-CH_2-$\underline{CH_2}$-CH_3), 23.77 (CH_2, cycloheptane), 23.85(CH_2, cycloheptane), 27.53 (C5'H_2), 29.37 (CH_2, cycloheptane), 29.49 (CH_2, cycloheptane), 31.06 (C2'-$\underline{(CH_3)_b}$), 33.76 (S-$\underline{CH_2}$-CH_2-CH_3), 35.24 (CH_2, cycloheptane), 35.75 (CH_2, cycloheptane), 37.53 (C3'H_2), 39.80 (C5), 40.06 (C_6H_2), 54.69 (C4'H), 60.25 (C6'H_2), 71.73 (C2'), 124.13 (C Ar), 124.33 (CH Ar), 125.91 (CH Ar), 127.25 (CH Ar), 129.43 (CH Ar), 131.91 ($C4_a$), 136.26 (C Ar), 149.78 (C*10*$_b$), 157.56 (C*2*), 161.15 (C=O). Found, %: C 71.88; H 8.37; N 6.18; S 6.72. $C_{28}H_{38}N_2O_2S$. Calculated, %: C 72.06; H 8.21; N 6.00; S 6.87.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-(isopropylthio)-3H-spiro[benzo[h]quinazoline -5,1'-cycloheptan]-4(6H)-one (11), (R=i–C_3H_7):Yield 1.7 g (73%), mp 181–182°C, R_f=0.65 (ethylacetate-benzene–hexane,1:7:7): IR spectrum, ν, cm^{-1}. 1600.7 (C=C arom); 1662 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.25 (s, 3H, C2'-$(CH_3)_a$), 1.30 (s, 3H, C2'-$(CH_3)_b$), 1.31-1.42 (m, 2H, CH_2, cycloheptane), 1.45-1.87 (m, 10H, 5×CH_2, cycloheptane), 1.52 (d, 6H, J=6.94, S-CH-$\underline{(CH_3)_2}$), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.68-2.80 (m, 1H, C3'H_b), 2.86 (s, 2H, C_6H_2), 2.87-3.02 (m, 1H, C5'H_b), 3.61-3.74 (m, 1H, C6'H_a), 3.76-3.85 (m, 1H, C6'H_b), 4.12 (sp, 1H, J=6.94, S-$\underline{CH}$-$(CH_3)_2$), 4.40-4.63 (m, 1H, C4'H), 7.12-7.17 (m, 1H, CH Ar), 7.20-7.32 (m, 2H, 2×CH Ar), 7.90-7.96 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 21.30 (C2'-$\underline{(CH_3)_a}$), 22.21 (S-CH-$\underline{(CH_3)_2}$), 23.76 (CH_2, cycloheptane), 23.85(CH_2, cycloheptane), 27.48 (C5'H_2), 29.37 (CH_2, cycloheptane), 29.49 (CH_2, cycloheptane), 31.06 (C2'-$\underline{(CH_3)_b}$), 35.28 (CH_2, cycloheptane), 35.75 (CH_2, cycloheptane), 37.47 (S-$\underline{CH}$-$(CH_3)_2$), 37.53 (C3'H_2), 39.81 (C5), 40.07 (C6H_2), 54.69 (C4'H), 60.21 (C6'H_2), 71.73 (C2'), 124.15 (C Ar), 124.32 (CH Ar), 125.95 (CH Ar), 127.26 (CH Ar), 129.43 (CH Ar), 131.92 ($C4_a$), 136.26 (C Ar), 149.88 ($C10_b$), 157.51 (C2), 161.11 (C=O). Found, %: C 71.88; H 8.37; N 6.18; S 6.72. $C_{28}H_{38}N_2O_2S$. Calculated, %: C 72.06; H 8.21; N 6.00; S 6.87.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-(isopentylthio)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one (12), (R=i-C_5H_{11}): Yield 2.0 g (81%), mp 137–138°C, R_f 0.61 (ethylacetate-benzene–hexane, 1:5:7):IR spectrum, ν, cm^{-1}. 1602.7 (C=C arom); 1665 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.01 (d, 6H, J=6.40, S-CH_2-CH_2-CH-$\underline{(CH_3)_2}$), 1.25 (s, 3H, C2'-$(CH_3)_a$), 1.30 (s, 3H, C2'-$(CH_3)_b$), 1.30-1.42 (m, 2H, CH_2, cycloheptane), 1.45-1.88 (m, 13H, 5×CH_2,

cycloheptane), S-CH_2-CH_2-CH-$(CH_3)_2$, S-CH_2-CH_2-CH-$(CH_3)_2$), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.67-2.80 (m, 1H, C3'H_b), 2.86 (s, 2H, C_6H_2), 2.87-3.02 (m, 1H, C5'H_b), 3.22-3.33 (m, 2H, S-CH_2-CH_2-CH-$(CH_3)_2$), 3.58-3.72 (m, 1H, C6'H_a), 3.75-3.85 (m, 1H, C6'H_b), 4.45-4.65 (m, 1H, C4'H), 7.11-7.17 (m, 1H, CH Ar), 7.19-7.32 (m, 2H, 2×CH Ar), 7.92-7.99 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 21.24 (C2'-$(CH_3)_a$), 21.86 (S-CH_2-CH_2-CH-$(CH_3)_2$), 23.76 (CH_2, cycloheptane), 23.84 (CH_2, cycloheptane), 27.20 (S-CH_2-CH_2-CH-$(CH_3)_2$), 27.51 (C5'H_2), 29.36 (CH_2, cycloheptane), 29.48 (CH_2, cycloheptane), 29.99 (S-CH_2-CH_2-CH-$(CH_3)_2$), 31.05 (C2'-$(CH_3)_b$), 35.24 (CH_2, cycloheptane), 35.75 (CH_2, cycloheptane), 37.19 (S-CH_2-CH_2-CH-$(CH_3)_2$), 37.52 (C3'H_2), 39.81 (C5), 40.03 (C_6H_2), 54.76 (C4'H), 60.24 (C6'H_2), 71.73 (C2'), 124.12 (C Ar), 124.37 (CH Ar), 125.80 (CH Ar), 127.25 (CH Ar), 129.44 (CH Ar), 131.87 ($C4_a$), 136.25 (C Ar), 149.80 ($C10_b$), 157.54 (C2), 161.13 (C=O). Found, %: C 72.98; H 8.38; N 5.82; S 6.31. $C_{30}H_{42}N_2O_2S$. Calculated, %: C 72.83; H 8.56; N 5.66; S 6.48.

2-(Allylthio)-3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-3H-spiro[benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one (13), (R=$CH_2CH=CH_2$): Yield 1.95 g (84%), mp 149–150°C, R_f 0.67 (ethylacetate-benzene–hexane, 1:7:7). IR spectrum, ν, cm^{-1}. 1605 (C=C arom); 1664 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.25 (s, 3H, C2'-$(CH_3)_a$), 1.30 (s, 3H, C2'-$(CH_3)_b$), 1.31-1.42 (m, 2H, CH_2, cycloheptane), 1.45-1.87 (m, 10H, 5×CH_2, cycloheptane), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.67-2.79 (m, 1H, C3'H_b), 2.85-3.02 (m, 1H, C5'H_b), 2.87 (s, 2H, C_6H_2), 3.60-3.73 (m, 1H, C6'H_a), 3.75-3.85 (m, 1H, C6'H_b), 3.96 (d, 2H, J=7.09, S-CH_2-CH=CH_2), 4.43-4.65 (m, 1H, C4'H), 5.17-5.23 (m, 1H, S-CH_2-CH=CH_a), 5.33-5.43 (m, 1H, S-CH_2-CH=CH_b), 5.94-6.10 (m, 1H, S-CH_2-CH=CH_2), 7.12-7.18 (m, 1H, CH Ar), 7.21-7.33 (m, 2H, 2×CH Ar), 7.94-8.00 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 21.23 (C2'-$(CH_3)_a$), 23.76 (CH_2, cycloheptane), 23.85(CH_2, cycloheptane), 27.55 (C5'H_2), 29.36 (CH_2, cycloheptane), 29.48 (CH_2, cycloheptane), 31.05 (C2'-$(CH_3)_b$), 34.62 (S-CH_2-CH=CH_2), 35.22 (CH_2, cycloheptane), 35.72 (CH_2, cycloheptane), 37.57 (C3'H_2), 39.82 (C5), 40.02 ($C6H_2$), 55.03 (C4'H), 60.21 (C6'H_2), 71.73 (C2'), 118.40 (S-CH_2-CH=CH_2), 124.26 (C Ar), 124.46 (CH Ar), 125.97 (CH Ar), 127.25 (CH Ar), 129.50 (CH Ar), 131.79 ($C4_a$), 132.10 (S-CH_2-CH=CH_2), 136.24 (C Ar), 149.81 ($C10_b$), 156.97 (C2), 161.07 (C=O). Found, %: C 72.21; H 7.65; N 6.22; S 6.72. $C_{28}H_{36}N_2O_2S$. Calculated, %: C 72.38; H 7.81; N 6.03; S 6.90.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-((2-methylallyl)thio)-3H-spiro [benzo[h]-quinazoline-5,1'-cycloheptan]-4(6H)-one (14), (R=$CH_2C(CH_3)=CH_2$): Yield 2.0 g (83%), mp 164–165°C, R_f 0.65 (ethylacetate-benzene–hexane, 1:7:7): IR spectrum, ν, cm^{-1}. 1605 (C=C arom); 1654 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.26 (s, 3H, C2'-$(CH_3)_a$), 1.31 (s, 3H, C2'-$(CH_3)_b$), 1.31-1.42 (m, 2H, CH_2, cycloheptane), 1.45-1.87 (m, 10H, 5×CH_2, cycloheptane), 1.90 (s, 3H, S-CH_2-C(CH_3)=CH_2), 2.18-2.40 (m, 2H, C3'H_a, C5'H_a), 2.68-2.81 (m, 1H, C3'H_b), 2.85-3.03 (m, 1H, C5'H_b), 2.87 (s, 2H, C_6H_2), 3.61-3.74 (m, 1H, C6'H_a), 3.76-3.86 (m, 1H, C6'H_b), 3.98 (d, 1H, J=13.19, S-CH_a-$C(CH_3)=CH_2$), 4.03 (d, 1H, J=13.19, S-CH_b-$C(CH_3)=CH_2$), 4.48-

4.68 (m, 1H, C4'H), 4.92-4.96 (m, 1H, S-CH_2-C(CH_3)=$\underline{CH_a}$), 5.08-5.12 (m, 1H, S-CH_2-C(CH_3)=$\underline{CH_b}$), 7.12-7.18 (m, 1H, CH Ar), 7.21-7.33 (m, 2H, 2×CH Ar), 7.94-8.00 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 21.06 (S-CH_2-C($\underline{CH_3}$)=CH_2), 21.27 (C2'-$(\underline{CH_3})_a$), 23.75 (CH_2, cycloheptane), 23.83(CH_2, cycloheptane), 27.54 (C5'H_2), 29.35 (CH_2, cycloheptane), 29.47 (CH_2, cycloheptane), 31.04 (C2'-$(\underline{CH_3})_b$), 35.19 (CH_2, cycloheptane), 35.70 (CH_2, cycloheptane), 37.57 (C3'H_2), 38.78 (S-$\underline{CH_2}$-C(CH_3)=CH_2), 39.81 (C5), 39.99 (C_6H_2), 55.11 (C4'H), 60.21 (C6'H_2), 71.73 (C2'), 114.87 (S-CH_2-C(CH_3)=$\underline{CH_2}$), 124.25 (C Ar), 124.46 (CH Ar), 125.91 (CH Ar), 127.25 (CH Ar), 129.47 (CH Ar), 131.76 ($C4_a$), 136.23 (C Ar), 138.89 (S-CH_2-$\underline{C}$(CH_3)=CH_2), 149.70 ($C10_b$), 157.17 (C2), 161.08 (C=O). Found, %: C 72.57; H 8.18; N 5.68; S 6.88. $C_{29}H_{38}N_2O_2S$. Calculated, %: C 72.76; H 8.00; N 5.85; S 6.70.

2-(Benzylthio)-3-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-3H-spiro [benzo[h]quinazoline-5,1'-cycloheptan]-4(6H)-one (15), (R=$CH_2C_6H_5$):Yield 2.2 g (85%), mp 173–174°C, R_f 0.68 (ethylacetate-benzene–hexane, 1:7:7): IR spectrum, ν, cm^{-1}. 1605 (C=C arom); 1662 (C=O). ^{1}H NMR spectrum, δ, ppm. 1.24 (s, 3H, C2'-$(CH_3)_a$), 1.27 (s, 3H, C2'-$(CH_3)_b$), 1.32-1.44 (m, 2H, CH_2, cycloheptane), 1.45-1.88 (m, 10H, 5×CH_2, cycloheptane), 2.20-2.39 (m, 2H, C3'H_a, C5'H_a), 2.66-2.79 (m, 1H, C3'H_b), 2.85-3.00 (m, 1H, C5'H_b), 2.87 (s, 2H, C_6H_2), 3.58-3.70 (m, 1H, C6'H_a), 3.74-3.83 (m, 1H, C6'H_b), 4.43-4.62 (m, 1H, C4'H), 4.52 (d, 1H, J=13.02, S-CH_a), 4.59 (d, 1H, J=13.02, S-CH_b), 7.13-7.18 (m, 1H, CH Ar), 7.20-7.35 (m, 5H, 5×CH Ar), 7.39-7.45 (m, 2H, 2×CH Ar), 7.98-8.03 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 21.28 (C2'-$(\underline{CH_3})_a$), 23.76 (CH_2, cycloheptane), 23.84(CH_2, cycloheptane), 27.53 (C5'H_2), 29.35 (CH_2 cycloheptane), 29.46 (CH_2 cycloheptane), 31.03 (C2'-$(\underline{CH_3})_b$), 35.22 (CH_2, cycloheptane), 35.69 (CH_2, cycloheptane), 36.51 (S-CH_2), 37.53 (C3'H_2), 39.84 (C5), 40.00 (C_6H_2), 54.93 (C4'H), 60.16 (C6'H_2), 71.70 (C2'), 124.41 (C Ar), 124.59 (CH Ar), 125.95 (CH Ar), 127.04 (CH Ar), 127.25 (CH Ar), 128.06 (2×CH Ar), 128.67 (2×CH Ar), 129.51 (CH Ar), 131.76 ($C4_a$), 135.21 (C Ar), 136.22 (C Ar), 149.81 ($C10_b$), 157.34 (C2), 161.03 (C=O). Found, %: C 74.50; H 7.62; N 5.27; S 6.39. $C_{32}H_{38}N_2O_2S$. Calculated, %: C 74.67; H 7.44; N 5.44; S 6.23.

3-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-2-((2-methylbenzyl)thio)-3H-spiro[benzo[h]-quinazoline-5,1'-cycloheptan]-4(6H)-one (16), (R=2–$CH_3C_6H_4CH_2$): Yield 2.1 g (79%), mp 182–183°C, R_f 0.64 (ethylacetate-benzene–hexane 1:7:7): IR spectrum, ν, cm^{-1}. 1603 (C=C arom); 1661.7 (C=O). ^{1}H NMR spectrum, δ, ppm. 24 (s, 3H, C2'-$(CH_3)_a$), 1.25 (s, 3H, C2'-$(CH_3)_b$), 1.32-1.44 (m, 2H, CH_2, cycloheptane), 1.46-1.89 (m, 10H, 5×CH_2, cycloheptane), 2.22-2.40 (m, 2H, C3'H_a, C5'H_a), 2.45 (s, 3H, $\underline{CH_3}$-Ph), 2.68-2.80 (m, 1H, C3'H_b), 2.85-3.00 (m, 1H, C5'H_b), 2.88 (s, 2H, C_6H_2), 3.57-3.69 (m, 1H, C6'H_a), 3.73-3.83 (m, 1H, C6'H_b), 4.40-4.61 (m, 1H, C4'H), 4.52 (d, 1H, J=12.87, S-CH_a), 4.57 (d, 1H, J=12.87, S-CH_b), 7.08-7.38 (m, 7H, 7×CH Ar), 7.99-8.05 (m, 1H, CH Ar). ^{13}C NMR spectrum, δ_C, ppm: 18.72 ($\underline{CH_3}$-Ph), 21.31 (C2'-$(\underline{CH_3})_a$), 23.77 (CH_2, cycloheptane), 23.86 (CH_2, cycloheptane), 27.53 (C5'H_2), 29.36 (CH_2, cycloheptane), 29.47 (CH_2, cycloheptane), 31.03 (C2'-$(\underline{CH_3})_b$), 35.22 (CH_2, cycloheptane), 35.25 (S-CH_2), 35.69

(CH_2, cycloheptane), 37.52 (C3'H_2), 39.86 (C5), 40.02 (C_6H_2), 54.70 (C4'H), 60.15 (C6'H_2), 71.69 (C2'), 124.38 (C Ar), 124.58 (CH Ar), 125.79 (CH Ar), 125.96 (CH Ar), 127.26 (CH Ar), 127.55 (CH Ar), 129.53 (CH Ar), 129.84 (CH Ar), 129.97 (CH Ar), 131.82 ($C4_a$), 132.25 (C Ar), 136.25 (C Ar), 136.39 (C Ar), 149.84 ($C10_b$), 157.50 (C2), 161.03 (C=O). Found, %: C 74.81; H 7.82; N 5.48; S 6.24. $C_{33}H_{40}N_2O_2S$. Calculated, %: C 74.96; H 7.63; N 5.30; S 6.06.

3-(2,2-ԴԻՄԵԹԻԼՏԵՏՐԱՀԻԴՐՕ-2H-ՊԻՐԱՆ-4-ԻԼ)ՍՊԻՐՕ [ԲԵՆԶՕ[h]ԽԻՆԱԶՕԼԻՆ-5,1'-ՑԻԿԼՕՀԵՊՏԱՆ]-4 (6H)-ՕՆՆԵՐԻ ՍԻՆԹԵԶԸ ԵՎ ՀԱԿԱՕՒՌՈՒՑՔԱՅԻՆ ՀԱՏԿՈՒԹՅՈՒՆՆԵՐԸ

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Էթիլ 2-ցիանո-2-ցիկլոհեպտիլիդենացետատին բենզիլմագնեզիում քլորիդի ռեգիոսելեկտիվ միացումը հանգեցրել է 2-(1-բենզիլցիկլհեպտիլ)-2-ցիանոացետատի, որի ցիկլումն օգտագործվել է էթիլ 4'-ամինո-'H-սպիրո[ցիկլոհեպտան-1,2'-նավթալին]-3'-կարբոքսիլատի (ամինոէսթեր) սինթեզի համար: Ամինոէսթերի և 4-իզոթիոցիանատո-2,2-դիմեթիլտետրահիդրո-2H-պիրանի փոխազդեցությունից ստացված թիոուրեիդոածանցյալն, առանց ռեակցիոն միջավայրից անջատելու, ենթարկվել է ցիկլման, ինչը բերել է 3-(2,2-դիմեթիլտետրահիդրո-2H-պիրան-4-իլ)-2-թիօքսո-2,3-դիհիդրո-1H-սպիրո[բենզո[h]խինազոլին-5,1'-ցիկլոհեպտան]-4(6H)-ոնի սինթեզին: Թիօքսոածանցյալը հիմքի ներկայությամբ փոխազդում է հալոգենիդների հետ, որի արդյունքում ստացվում են 2-սուլֆանիլ-տեղակալված 3-(2,2-դիմեթիլտետրահիդրո-2H-պիրան-4-իլ)-3H-սպիրո[բենզո[h]խինազոլին-5,1'-ցիկլոհեպտան]-4(6H)-ոններ: Ուսումնասիրվել է սինթեզված միացությունների հակաուռուցքային և հակաբակտերիալ ակտիվությունը:

СИНТЕЗ И ПРОТИВООПУХОЛЕВЫЕ СВОЙСТВА 3-(2,2-ДИМЕТИЛТЕТРАГИДРО-2H-ПИРАН-4-ИЛ)СПИРО[БЕНЗО[h]ХИНАЗОЛИН-5,1'-ЦИКЛОГЕПТАН]-4 (6H)-ОНОВ

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Региоселективное присоединение бензилмагнийхлорида к этил-2-циано-2-циклогептилиденацетату привело к 2-1-бензилциклогептил)-2-цианоацетату, циклизация которого использовали для синтеза этил-4'-амино-1'H-спиро[циклогептан-1,2'-нафталин]-3'-карбоксилата (аминоэфир). Реакцией аминоэфира с 4-изотиоцианато-2,2-диметилтетрагидро-2H-пираном было получено соответствующее тиореидопроизводное, которое без выделения из реакционной среды подвергалось циклизации, что привело к синтезу 3-(2,2-диметилтетрагидро-2H-пиран-4-ил)-2-тиоксо-2,3-дигидро-1H-спиро[бензо[h]хиназолин-5,1'-циклогептан]-4(6H)-она. В присутствии оснований тиоксопроизводное реагирует с галогенидами, что приво-

дит к образованию 2-сульфанилзамещенных 3-(2,2-диметилтетрагидро-2H-пиран-4-ил)-3H-спиро[бензо[h]хиназолин-5,1'- циклогептан]-4(6H)-онов. Изучены противоопухолевая и антибактериальная активности синтезированных соединений.

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