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SYNTHESIS AND BIOLOGICAL ACTIVITY OF NEW DERIVATIVES OF PYRANO[3-4-c][1,2,4]TRIAZOLO[4,3-a]PYRIDINES

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A new method for obtaining new heterocyclic systems – S-alkyl substituted pyrano[3-4-c]-[1,2,4]triazolo[4,3-a]pyridines on the basis of 8-hydrazino derivatives of pyrano[3,4-c]pyridines has been developed. Alkylation of 3-thioxopyrano[3,4-c][1,2,4]triazolo[4,3-a]pyridines with different alkylhalogenids resulted in the synthesis of S-alkylpyrano[3-4-c]-[1,2,4]triazolo[4,3-a]pyridine derivatives. The antimicrobial and neurotropic activities of the synthesized compounds have been investigated.

References 13.

Condensed pyridines have a broad spectrum of biological activity. In particular, derivatives of pyranopyridines have shown antimicrobial, anti-inflammatory, anticonvulsant activities [1-4].

At the same time, tricyclic triazolopyridines are little studied, there is only one report in the literature on the synthesis of 1,2,4-triazolo[4,3-a]pyrano[3,2-e]pyridines, which have antihypertensive action [5].

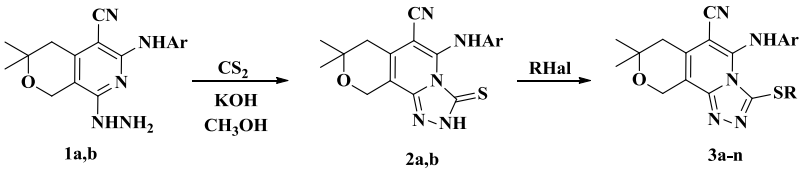
In continuation of studies on the synthesis of condensed pyridines [6,7] and with the purpose to study their biological activities we synthesized new S-alkyl substituted derivatives of pyrano[3,4-c][1,2,4]triazolo[4,3-a]pyridines **3a-n,** which are the derivatives of new heterocyclic systems.

As the starting material we used the 8-hydrazinopyrano[3,4-c]pyridines **1a,b**, which have been synthesized by us in the work [8].

In this work we developed a new method for obtaining 3-thioxopyrano[3,4-c][1,2,4]triazolo[4,3-a]pyridines **2a,b** by the interaction of compounds 1a,b with CS_2 in MeOH in the presence of KOH. A new method allowed to exclude pyridine from the reaction medium and increase the rate of cyclizations in contrast to work [8].

The obtained 3-thioxopyrano[3,4-c][1,2,4]triazolo[4,3-a]pyridines were transformed to the S-alkyl substituted derivatives **3a-n** under the action of different alkyl halogenids (Scheme).

Scheme



1a,b 2a,b 3a-n

Ar = C_6H_5 (1a, 2a, 3a-g); Ar = 4-$CH_3C_6H_4$ (1b, 2b, 3h-n);
3: R = $CH_2CON(C_2H_5)_2$ (a,k); CH_2-benzimidazol-2-yl (b); $CH_2CONHCH_2C_6H_5$ (c); $CH_2CONHCH_2$-4-$CH_3C_6H_4$ (d); CH_2CONH-3-ClC_6H_4 (e); CH_2CONH-2-$NO_2C_6H_4$ (f); CH_2CONH-1,3-thiazol-2-yl (g); $CH_2C_6H_5$ (h); $CH_2COC_6H_5$ (i); CH_2CONH-3-$CH_3C_6H_4$ (j); CH_2CONH-4-$COCH_3C_6H_4$ (l); CH_2CONH-2-naphthyl (m); CH_2CONH_2 (n)

The IR spectrum of compounds **3a–n** revealed the presence of absorption bands at 3306–3408 cm^{-1} assigned to NH group, and a strong absorption band at 2208–2226 cm^{-1} for C≡N group.

^{1}H NMR spectrum revealed the presence of signals at δ 3.92–4.88 ppm for SCH_2 protons. ^{13}C NMR spectra of compounds **3a,i,j,l** showed signals at δ 39.4-42.3 ppm corresponding to the SCH_2 group. The spectral data confirmed formation of *S*-alkyl derivatives [9]. The regioselectivity of this reaction was explained by the greater polarizability of the sulfur atom compared to the nitrogen atom [10].

The antimicrobial activity of compounds **3a–n** was studied by the agar diffusion assay [11]. Experiments were performed with Gram-positive staphylococci (*Staphylococcus aureus* 209P, JC-1) and Gram-negative rods (*Shigella dysenteriae flexneri* 6858, *Escherichia coli* 0-55). The studies showed that compounds **3a,b,f,g,j,k-n** had weak activity against all tested microbial strains: the diameters (d) of growth inhibition zones were 10–15 *mm*. The indicated compounds were significantly less active than the reference drug furazolidone (d 24–25 *mm*) [12].

Neurotropic activity of the newly synthesized triazolopyridine derivatives **3a-n** was studied by indicators characterizing the anticonvulsant activity and side effects. A study of 14 compounds **3a-n** and a reference drug diazepam was carried out on 120 white mice weighing 18–24 *g*. Anticonvulsant activity of the compounds was assessed by the prevention of the seizure clonic component induced by subcutaneous injection of corazole (90 *mg/kg*) to mice [13]. Unwanted side effects in these animals, namely the central myorelaxant effect and impaired motor coordination were examined by the rotating rod method [13].

The compounds under investigation were injected in a dose range of 50 *mg/kg* intraperitoneally 45 min before injection of corazole in the form of a suspension with Tween 80 and ethosuximide – at a dose of 150 *mg/kg*.

The study of anticonvulsant action revealed that not all synthesized derivatives had the same anticorazole activity. Thus, compounds **3a, c, i, j, l** at a dose of 50 *mg/kg* prevented convulsions only in 20–40% of animals, while ethosuximide

showed a 50% efficiency only at a dose of 150 *mg/kg*. Moreover, studies of these compounds and ethosuximide at the mentioned doses did not reveal the muscle relaxation phenomena.

Experimental Section

All chemicals, reagents, and solvents were of commercially high purity grade purchased from Sigma-Aldrich. Melting points (mp) were determined on a "Boetius" microtable. They are expressed in degree centigrade (ºC). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian "Mercury 300VX" 300 (^{1}H) and 75.462 *MHz* (^{13}C) spectrometer. Chemical shifts were reported as δ (parts per million) relative to TMS (tetramethylsilane) as an internal standard. IR spectra were recorded on "Nicolet Avatar 330 FT-IR" spectrophotometer and the reported wave numbers are given in cm^{-1}. TLC analyses were performed on "Silufol UV-254" plates using pyridine–ethyl acetate, 2:1 (2), butanol–acetic acid–water, 4:2:5 (3) as eluent; spots were developed with iodine vapor.

General procedure for the synthesis of 3-thioxopyrano[3,4-c][1,2,4]-triazolo[4,3-a]- pyridines 2a,b. Compounds **1a,b** 4.5 *mmol* and 5*ml* of CS_2 were added to a solution of 0.3 *g* (5.4 *mmol*) of KOH in 50 *ml* of methanol. The mixture was refluxed for 5 *h*. After cooling, the obtained solution was acidified with 10% HCl, the formed crystals were filtered and recrystallized from 1:1 mixture of EtOH-$CHCl_3$. The spectral data of compounds **2a,b** corresponded to data in reference [8].

5-Anilino-8,8-dimethyl-3-thioxo-2,3,7,10-tetrahydro-8H-pyrano[3,4-c][1,2,4]triazolo[4,3-a]pyridine-6-carbonitrile (2a). Yield 1.42 g (90%), mp 259–260°C.

8,8-Dimethyl-5-(4-methylphenyl)amino-3-thioxo2,3,7,10-tetrahydro-8H-pyrano[3,4-c]- [1,2,4]triazolo[4,3-a]pyridine-6-carbonitrile (2b). Yield 1.50 g (91%), mp 238–239°C.

General procedure for alkylation of pyranotriazolothiones 3a–n. The appropriate 2 *mmol* of compounds **2a,b** was added to a solution of 112 *mg* (2 *mmol*) of KOH in a mixture of 2 *ml* of H_2O and 12 *ml* of EtOH. After complete dissolution, the appropriate 2 *mmol* of alkyl halide was added with cooling, and the reaction mixture was stirred for 6 h at room temperature. The obtained crystals were filtered off, washed with H_2O, dried, and recrystallized from a 2:1 mixture of EtOH–$CHCl_3$.

2-[(5-Anilino-6-cyano-8,8-dimethyl-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]- pyridin-3-yl)thio]-*N*,*N*-diethylacetamide (3a). Yield 0.75 *g* (81%), mp 228-229ºC, R_f 0.60. IR spectrum, *ν*, cm^{-1}: 1675 (C=O), 2226 (CN), 3306 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.08 t (3H, *J* = 7.1, CH_3); 1.19 t (3H, *J* = 7.1, CH_3); 1.35 s (6H, 2×CH_3); 2.63 s (2H, 7-CH_2); 3.34 q (2H, *J* = 7.1, NCH_2); 3.39 q (2H, *J* = 7.1, NCH_2); 4.24 s (2H, SCH_2); 4.86 s (2H, 10-CH_2); 6.97-7.03 m (3H, H_{Ar}); 7.26-7.32 m (2H, H_{Ar}); 10.05 s (1H, 5-NH). ^{13}C NMR spectrum, δ, ppm, *MHz*: 12.5 (CH_3), 13.7 (CH_3), 25.9 (2CH_3), 39.4 (CH_2), 39.8 (CH_2), 40.2 (CH_2), 41.6 (SCH_2), 57.8 (OCH_2), 69.8, 90.6 (C-6), 113.1 (CN), 115.4, 117.9 (2CH), 122.0

(CH), 128.6 (2CH), 132.0, 140.6, 141.5, 142.0, 148.3, 166.2 (CO). Found, %: C 62.13; H 6.03; N 18.23; S 6.78. $C_{24}H_{28}N_6O_2S$. Calculated, %: C 62.05; H 6.07; N 18.09; S 6.90.

5-Anilino-3-[(1*H*-benzimidazol-2-ylmethyl)thio]-8,8-dimethyl-7,10-dihydro-8*H*-pyrano- [3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridine-6-carbonitrile (3b). Yield 0.76 *g* (79%), mp 204-206ºC, R_f 0.62. IR spectrum, *ν*, *cm*$^{-1}$: 2210 (CN), 3325, 3408 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.34 s (6H, 2×CH_3); 2.62 t (2H, *J* = 1.8, 7-CH_2); 4.65 s (2H, SCH_2); 4.84 t (2H, *J* = 1.8, 10-CH_2); 6.94-7.00 m (3H, H_{Ar}); 7.08-7.13 m (2H, H_{Ar}); 7.22-7.30 m (2H, H_{Ar}); 7.42-7.48 m (2H, H_{Ar}); 10.34 brs (1H, NH); 12.19 br.s (1H, 5-NH). Found, %: C 64.97; H 4.85; N 20.43; S 6.54. $C_{26}H_{23}N_7OS$. Calculated, %: C 64.85; H 4.81; N 20.36; S 6.66.

2-[(5-Anilino-6-cyano-8,8-dimethyl-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]- pyridin-3-yl)thio]-*N*-benzylacetamide (3c). Yield 0.76 *g* (76%), mp 209-210 ºC, R_f 0.62. IR spectrum, *ν*, *cm*$^{-1}$: 1670 (CO), 2212 (CN), 3325, 3367 (NH), ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.36 s (6H, 2×CH_3); 2.65 s (2H, 7-CH_2); 3.99 s (2H, SCH_2); 4.29 d (2H, *J* = 5.8, NHC$\underline{H_2}$); 4.86 s (2H, 10-CH_2); 6.97-7.03 m (3H, H_{Ar}); 7.11-7.32 m (7H, H_{Ar}); 8.66 t (1H, *J* = 5.8, NH); 9.76 s (1H, 5-NH). Found, %: C 64.97; H 5.33; N 16.92; S 6.34. $C_{27}H_{26}N_6O_2S$. Calculated, %: C 65.04; H 5.26; N 16.86; S 6.43.

2-[(5-Anilino-6-cyano-8,8-dimethyl-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]- pyridin-3-yl)thio]-*N*-(4-methylphenyl)acetamide (3d). Yield 0.82 *g* (82%), mp 231-232ºC, R_f 0.58. IR spectrum, *ν*, *cm*$^{-1}$: 1666 (CO), 2208 (CN), 3327, 3372 (NH). ^{1}H NMR spectrum, δ, ppm: 1.34 s (6H, 2×CH_3); 2.29 s (3H, CH_3); 2.61 s (2H, 7-CH_2); 4.14 s (2H, SCH_2); 4.84 s (2H, 10-CH_2); 6.94-7.00 m (2H, H_{Ar}); 7.00-7.05 m (3H, H_{Ar}); 7.24-7.31 m (2H, H_{Ar}); 7.38-7.42 m (2H, H_{Ar}); 9.62 s (1H, NH); 10.07 s (1H, 5-NH). Found, %: C 64.97; H 5.33; N 16.92; S 6.34. $C_{27}H_{26}N_6O_2S$. Calculated, %: C 65.04; H 5.26; N 16.86; S 6.43.

2-[(5-Anilino-6-cyano-8,8-dimethyl-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]- pyridin-3-yl)thio]-*N*-(3-chlorophenyl)acetamide (3e). Yield 0.80 *g* (77%), mp 217-218ºC, R_f 0.61. IR spectrum, *ν*, *cm*$^{-1}$: 1668 (CO), 2208 (CN), 3325, 3372 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.35 s (6H, 2×CH_3); 2.63 t (2H, *J* = 1.9, 7-CH_2); 4.16 s (2H, SCH_2); 4.84 t (2H, *J* = 1.9, 10-CH_2); 6.91-7.00 m (4H, H_{Ar}); 7.21 t (1H, *J* = 8.2, H_{Ar}); 7.23-7.30 m (2H, H_{Ar}); 7.42 dd (1H, *J* = 8.2, 2.1, H_{Ar}); 7.69 t (1H, *J* = 2.1, H_{Ar}); 9.47 brs (1H, NH); 10.35 brs (1H, 5-NH). Found, %: C 60.28; H 4.54; N 16.23; S 6.09. $C_{26}H_{23}ClN_6O_2S$. Calculated, %: C 60.17; H 4.47; N 16.19; S 6.18.

2-[(5-Anilino-6-cyano-8,8-dimethyl-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridin-3-yl)thio]-*N*-(2-nitrophenyl)acetamide (3f). Yield 0.81 *g* (76%), mp 245-247ºC, R_f 0.64. IR spectrum, *ν*, *cm*$^{-1}$: 1350, 1540 (NO_2), 1665 (CO), 2210 (CN), 3328, 3367 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.35 s (6H, 2×CH_3); 2.63 s (2H, 7-CH_2); 4.22 s (2H, SCH_2); 4.84 s (2H, 10-CH_2); 6.88-6.99 m (3H, H_{Ar}); 7.21-7.33 m (3H, H_{Ar}); 7.63 t.d (1H, *J* = 8.3, 1.4, H_{Ar}); 7.98 dd (1H, *J* = 8.3, 1.4, H_{Ar}); 8.05 dd (1H, *J* = 8.3, 1.1, H_{Ar}); 9.37 brs (1H, NH); 10.67 brs (1H, 5-

NH). Found, %: C 58.85; H 4.41; N 18.44; S 6.13. $C_{26}H_{23}N_7O_4S$. Calculated, %: C 58.97; H 4.38; N 18.51; S 6.06.

2-[(5-Anilino-6-cyano-8,8-dimethyl-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]- pyridin-3-yl)thio]-*N*-1,3-thiazol-2-ylacetamide (3g). Yield 0.78 *g* (79%), mp 262-263ºC, R_f 0.59. IR spectrum, *v*, cm^{-1}: 1672 (CO), 2210 (CN), 3329, 3377 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.35 s (6H, 2×CH_3); 2.63 t (2H, *J* = 1.8, 7-CH_2); 4.21 s (2H, SCH_2); 4.84 t (2H, *J* = 1.8, 10-CH_2); 6.90-6.97 m (3H, H_{Ar}); 6.99 d (1H, *J* = 3.5, SCH); 7.22-7.29 m (2H, H_{Ar}); 7.37 dd (1H, *J* = 3.5, NCH); 9.37 brs (1H, NH); 12.29 brs (1H, 5-NH). Found, %: C 56.30; H 4.28; N 19.99; S 12.91. $C_{23}H_{21}N_7O_2S_2$. Calculated, %: C 56.19; H 4.31; N 19.94; S 13.05.

3-(Benzylthio)-8,8-dimethyl-5-[(4-methylphenyl)amino]-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridine-6-carbonitrile (3h). Yield 0.69 *g* (76%), mp 219-220ºC, R_f 0.61.IR spectrum, *v*, cm^{-1}: 2210 (CN), 3327 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.34 s (6H, 2×CH_3); 2.32 s (3H, CH_3); 2.60 t (2H, *J* = 1.7, 7-CH_2); 4.40 s (2H, SCH_2); 4.84 t (2H, *J* = 1.7, 10-CH_2); 6.70-6.75 m (2H, H_{Ar}); 7.01-7.06 m (2H, H_{Ar}); 7.18-7.27 m (5H, H_{Ar}); 8.98 brs (1H, 5-NH). Found, %: C 68.61; H 5.58; N 15.48; S 6.89. $C_{26}H_{25}N_5OS$. Calculated, %: C 68.55; H 5.53; N 15.37; S 7.04.

8,8-Dimethyl-5-[(4-methylphenyl)amino]-3-[(2-oxo-2-phenylethyl)thio]-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridine-6-carbonitrile (3i). Yield 0.77 *g* (80%), mp 201-202ºC, R_f 0.66. IR spectrum, *v*, cm^{-1}: 1685 (CO), 2210 (CN), 3322 (NH). ^{1}H NMR spectrum, δ, ppm: 1.35 s (6H, 2×CH_3); 2.32 s (3H, CH_3); 2.62 s (2H, 7-CH_2); 4.83 s (2H, 10-CH_2); 4.88 s (2H, SCH_2); 6.83-6.88 m (2H, H_{Ar}); 7.04-7.09 m (2H, H_{Ar}); 7.46-7.52 m (2H, H_{Ar}); 7.57-7.64 m (1H, H_{Ar}); 7.98-8.03 m (2H, H_{Ar}); 9.30 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.3 (CH_3), 25.9 (2CH_3), 36.4 (CH_2), 42.3 (SCH_2), 57.8 (OCH_2), 69.8, 91.8 (C-6), 113.1(CN), 116.1, 117.9 (2CH), 128.0 (2CH), 128.1 (2CH), 129.3 (2CH), 131.0 (CH), 131.6, 133.0, 135.1, 138.9, 141.8, 142.2, 148.4, 192.6 (CO). Found, %: C 67.15; H 5.28; N 14.54; S 6.49. $C_{27}H_{25}N_5O_2S$. Calculated, %: C 67.06; H 5.21; N 14.48; S 6.63.

2-({6-Cyano-8,8-dimethyl-5-[(4-methylphenyl)amino]-7,10-dihydro-8*H*-pyrano[3,4-*c*]-[1,2,4]triazolo[4,3-*a*]pyridin-3-yl}thio)-*N*-(3-methylphenyl)acetamide (3j). Yield 0.83 *g* (81%), mp 220-222ºC, R_f 0.60. IR spectrum, *v*, cm^{-1}: 1666 (CO), 2209 (CN), 3325, 3371 (NH). ^{1}H NMR spectrum, δ, ppm: 1.34 s (6H, 2×CH_3); 2.32 s (3H, CH_3); 2.33 s (3H, CH_3); 2.61 s (2H, 7-CH_2); 4.14 s (2H, SCH_2); 4.83 s (2H, 10-CH_2); 6.78-6.83 m (1H, H_{Ar}); 6.88-6.93 m (2H, H_{Ar}); 7.06-7.13 m (3H, H_{Ar}); 7.28-7.35 m (2H, H_{Ar}); 9.52 brs (1H, NH); 10.06 brs (1H, 5-NH). ^{13}C NMR spectrum, δ, ppm: 20.3 (CH_3), 21.0 (CH_3), 25.9 (2CH_3), 36.4 (CH_2), 39.8 (SCH_2), 57.7 (OCH_2), 69.8, 90.4 (C-6), 113.0 (CN), 115.2, 116.2 (CH), 118.4 (2CH), 119.5 (CH), 123.7 (CH), 127.8 (CH), 129.2 (2CH), 131.3, 132.1, 137.3, 138.1, 138.2, 141.9, 142.0, 148.4, 165.3 (CO). Found, %: C 65.43; H 5.47; N 16.51; S 6.34. $C_{28}H_{28}N_6O_2S$. Calculated, %: C 65.60; H 5.51; N 16.39; S 6.26.

2-({6-Cyano-8,8-dimethyl-5-[(4-methylphenyl)amino]-7,10-dihydro-8*H*-pyrano[3,4-*c*]-[1,2,4]triazolo[4,3-*a*]pyridin-3-yl}thio)-*N*,*N*-diethylacetamide (3k).

Yield 0.75 *g* (78%), mp 208-209ºC, R_f 0.65. IR spectrum, *ν*, *cm*$^{-1}$: 1675 (C=O), 2225 (CN), 3308 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.08 t (3H, *J* = 7.1, $CH_2C\underline{H_3}$); 1.19 t (3H, *J* = 7.1, $CH_2C\underline{H_3}$); 1.34 s (6H, 2×CH_3); 2.35 s (3H, CH_3); 2.61 s (2H, 7-CH_2); 3.34 q (2H, *J* = 7.1, NCH_2); 3.38 q (2H, *J* = 7.1, NCH_2); 4.23 s (2H, SCH_2); 4.83 s (2H, 10-CH_2); 6.92-6.97 m (2H, H_{Ar}); 7.08-7.13 m (2H, H_{Ar}); 10.07 brs (1H, 5-NH). Found, %: C 62.83; H 6.25; N 17.71; S 6.59. $C_{25}H_{30}N_6O_2S$. Calculated, %: C 62.74; H 6.32; N 17.56; S 6.70.

***N*-(4-Acetylphenyl)-2-({6-cyano-8,8-dimethyl-5-[(4-methylphenyl)amino]-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridin-3-yl}thio)acetamide (3l).** Yield 0.83 *g* (77%), mp 207-208ºC, R_f 0.62. IR spectrum, *ν*, *cm*$^{-1}$: 1665, 1710 (CO), 2208 (CN), 3325, 3373 (NH). ^{1}H NMR spectrum, δ, ppm: 1.34 s (6H, 2×CH_3); 2.33 s (3H, CH_3); 2.51 s (3H, $COCH_3$); 2.60 s (2H, 7-CH_2); 4.18 s (2H, SCH_2); 4.82 s (2H, 10-CH_2); 6.85-6.91 m (2H, H_{Ar}); 7.04-7.11 m (2H, H_{Ar}); 7.64-7.69 m (2H, H_{Ar}); 7.82-7.87 m (2H, H_{Ar}); 9.42 brs (1H, NH); 10.50 brs (1H, 5-NH). ^{13}C NMR spectrum, δ, ppm: 20.3 (CH_3), 25.7 (CH_3), 25.9 (2CH_3), 36.4 (CH_2), 39.4 (SCH_2), 57.7 (OCH_2), 69.8, 91.2 (C-6), 113.0 (CN), 115.6, 118.1 (2CH), 118.2 (2CH), 128.8 (2CH), 129.2 (2CH), 131.2, 131.8, 131.9, 138.5, 141.8, 142.1, 142.5, 148.4, 165.9, 194.6 (CO). Found, %: C 64.56; H 5.18; N 15.62; S 5.81. $C_{29}H_{28}N_6O_3S$. Calculated, %: C 64.43; H 5.22; N 15.54; S 5.93.

2-({6-Cyano-8,8-dimethyl-5-[(4-methylphenyl)amino]-7,10-dihydro-8*H*-pyrano[3,4-*c*][1,2,4]triazolo[4,3-*a*]pyridin-3-yl}thio)-*N*-2-naphthylacetamide (3m). Yield 0.82 *g* (75%), mp 249-250ºC, R_f 0.65. IR spectrum, *ν*, *cm*$^{-1}$: 1670 (CO), 2208 (CN), 3323, 3370 (NH). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.34 s (6H, 2×CH_3); 2.32 s (3H, CH_3); 2.60 brs (2H, 7-CH_2); 4.31 s (2H, SCH_2); 4.86 brs (2H, 10-CH_2); 6.84-6.89 m (2H, H_{Ar}); 7.03-7.08 m (2H, H_{Ar}); 7.40-7.50 m (3H, H_{Ar}); 7.66 brd (1H, *J* = 8.1, H_{Ar}); 7.76 brd (1H, *J* = 7.5, H_{Ar}); 7.79-7.85 m (1H, H_{Ar}); 8.00-8.06 m (1H, H_{Ar}); 9.48 brs (1H, NH); 10.20 brs (1H, 5-NH). Found, %: C 67.95; H 5.19; N 15.21; S 5.92. $C_{31}H_{28}N_6O_2S$. Calculated, %: C 67.86; H 5.14; N 15.32; S 5.84.

2-({6-Cyano-8,8-dimethyl-5-[(4-methylphenyl)amino]-7,10-dihydro-8*H*-pyrano[3,4-*c*]- [1,2,4]triazolo[4,3-*a*]pyridin-3-yl}thio)acetamide (3n). Yield 0.69 *g* (82%), mp 250-252ºC, R_f 0.67. IR-spectrum, *ν*, *cm*$^{-1}$: 1675 (CO), 2210 (CN), 3325 (NH), 3370, 3424 (NH_2). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.34 s (6H, 2×CH_3); 2.34 s (3H, CH_3); 2.60 t (2H, *J* = 1.8, 7-CH_2); 3.92 s (2H, SCH_2); 4.83 t (2H, *J* = 1.8, 10-CH_2); 6.91-6.96 m (2H, H_{Ar}); 7.07-7.12 m (2H, H_{Ar}); 7.15 brs (1H, NH_2); 7.61 brs (1H, NH_2); 9.87 brs (1H, 5-NH). Found, %: C 59.81; H 5.20; N 19.97; S 7.50. $C_{21}H_{22}N_6O_2S$. Calculated, %: C 59.70; H 5.25; N 19.89; S 7.59.

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ՆՈՐ ՊԻՐԱՆՈ[3,4-c][1,2,4]ՏՐԻԱԶՈԼՈ[4,3-a]ՊԻՐԻԴԻՆՆԵՐԻ ԱԾԱՆՑՅԱԼՆԵՐԻ ՍԻՆԹԵԶԸ ԵՎ ԿԵՆՍԱԲԱՆԱԿԱՆ ԱԿՏԻՎՈՒԹՅՈՒՆԸ

Ե. Գ. ՊԱՐՈՆԻԿՅԱՆ, Շ. Շ. ԴԱՇՅԱՆ, Ն. Ս. ՄԻՆԱՍՅԱՆ, Ա. Գ. ՀԱԿՈԲՅԱՆ և Հ. Մ. ՍՏԵՓԱՆՅԱՆ

Մշակված է նոր հետերոցիկլիկ համակարգի – 3-թիօքսոպիրանո[3,4-c][1,2,4]–տրիազոլո-[4,3-a]–պիրիդինների ածանցյալների ստացման եղանակ՝ 8-հիդրազինոպիրանո[3,4-c]պիրիդինների փոխազդեցությամբ ածխածնահանձնի հետ, կալիումի հիդրօքսիդի մեթանոլային լուծույթի ներկայությամբ: Նոր եղանակը հնարավորություն է տալիս բացառել ռեակցիոն միջավայրում պիրիդինի առկայությունը և զգալիորեն մեծացնել ցիկլման ռեակցիայի արագությունը:

3-Թիօքսոպիրանո[3,4-c][1,2,4]տրիազոլո[4,3-a]պիրիդինների ալկիլացմամբ, տարբեր ալկիլ հալոգենիդներով, սինթեզված են S-ալկիլպիրանո[3,4-c][1,2,4]տրիազոլո[4,3-a]պիրիդինների ածանցյալներ: Ուսումնասիրված են սինթեզված միացությունների հակամանրէային և նեյրոտրոպ ակտիվությունները: Ուսումնասիրությունների արդյունքում պարզվել է, որ որոշ հետազոտվող միացություններ ցուցաբերում են հակամանրէային և նեյրոտրոպ ակտիվություններ:

СИНТЕЗ И БИОЛОГИЧЕСКАЯ АКТИВНОСТЬ НОВЫХ ПРОИЗВОДНЫХ ПИРАНО[3,4-c][1,2,4]ТРИАЗОЛО[4,3-a]ПИРИДИНОВ

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Разработан новый метод получения производных 3-тиоксопирано[3,4-c][1,2,4]триазоло[4,3-a]пиридинов взаимодействием 8-гидразинопирано[3,4-c]пиридинов с сероуглеродом в присутствии метанольного раствора гидроксида калия. Новый метод позволил исключить из реакционной среды пиридин и увеличить скорость циклизации. Алкилированием 3-тиоксопирано[3,4-c][1,2,4]триазоло[4,3-a]пиридинов с различными алкилгалогенидами синтезированы производные *S*-алкилпирано[3,4-c][1,2,4]триазоло[4,3-a]пиридинов. Изучена антимикробная и нейротропная активность синтезированных соединений. Исследования показали, что некоторые производные новой гетероциклической системы оказывают антимикробное и нейротропное действие.

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