Chemistry of Heterocyclic Compounds, Vol. 46, No. 8, 2010

CONDENSED ISOQUINOLINES. 35*. SYNTHESIS AND REACTIONS OF 4H-THIENO[3',4':5,6]PYRIMIDO-[1,2-*b*]ISOQUINOLINE-4,11(5H)-DIONE

A. V. Zadorozhny[1], V. A. Kovtunenko[1], and A. V. Turov[1]**

Derivatives of the previously unknown tetracyclic system 4H-thieno[3',4':5,6]pyrimido[1,2-b]isoquinoline-4,11(5H)-dione have been synthesized. A comparison of the spectral characteristics and the biological activities of these compounds has been carried out, and also of their positional isomers and benzene isosteres. The differences, associated with the position of the sulfur atom, are most reflected in their electronic spectra.

Keywords: positional isomers, derivatives of 4H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinoline-4,11(5H)-dione, nucleophilic substitution, calculation of biological activity, UV spectra, cyclization.

The present work is a continuation of our investigations in the field of derivatives of thieno[3,4-*d*]-, thieno[2,3-*d*]-, thieno[3,2-*d*]pyrimidin-4-ones and quinazolin-4-ones, referred to series **A,B,C,** and **D** respectively. Previously we described *ortho*-(4-oxo-3,4-dihydrothienopyrimidin-2-ylmethyl)benzoic acids **1A** [2], **1B**, **1C** [3] and also *ortho*-(4-oxo-3,4-dihydroquinazolin-2-ylmethyl)benzoic acid **1D** [4].

The products of their intramolecular cyclization at atom N(1) – **2B-2D** [5] were obtained from acids **1B-1D** by boiling in acetic anhydride. In the present work thienopyrimidoisoquinolinedione **2A** was synthesized by cyclization of acid **1A** under analogous conditions. Treatment of the latter with $POCl_3$ in the presence of a catalytic amount of pyridine gave the 4-chloro-substituted product **3A**, from which by treatment with cyclic amines (pyrrolidine, piperidine, morpholine) and sodium methoxide the corresponding derivatives at position 4 were obtained – **4A-7A** – and by treatment with thiourea – 4-thioxo-4,5-dihydrothienopyrimidoisoquinolin-11-one, **8A**. Alkylation of compound **8A** (MeI/MeONa) gave 4-methylthiothienopyrimidoisoquinolin-11-one **9A**.

The structure of compound **2A** – the starting material for the synthesis of **3A-9A,** was demonstrated by various methods. For example, quantum-chemical calculations of the energies of the isomeric systems **2A** and **10A** were carried out using the HyperChem Professional 5.1 computer programs [6] in the *ab initio* method in the basis set 3-21 G** (including *d*-orbitals) with complete optimization of the geometry gave a value of 743238.8 for molecule **2A** and 743227.6 kcal·mol^{-1} for molecule **10A**. Thus intramolecular cyclization at atom N(1) for acid **1A** is a thermodynamically favorable process.

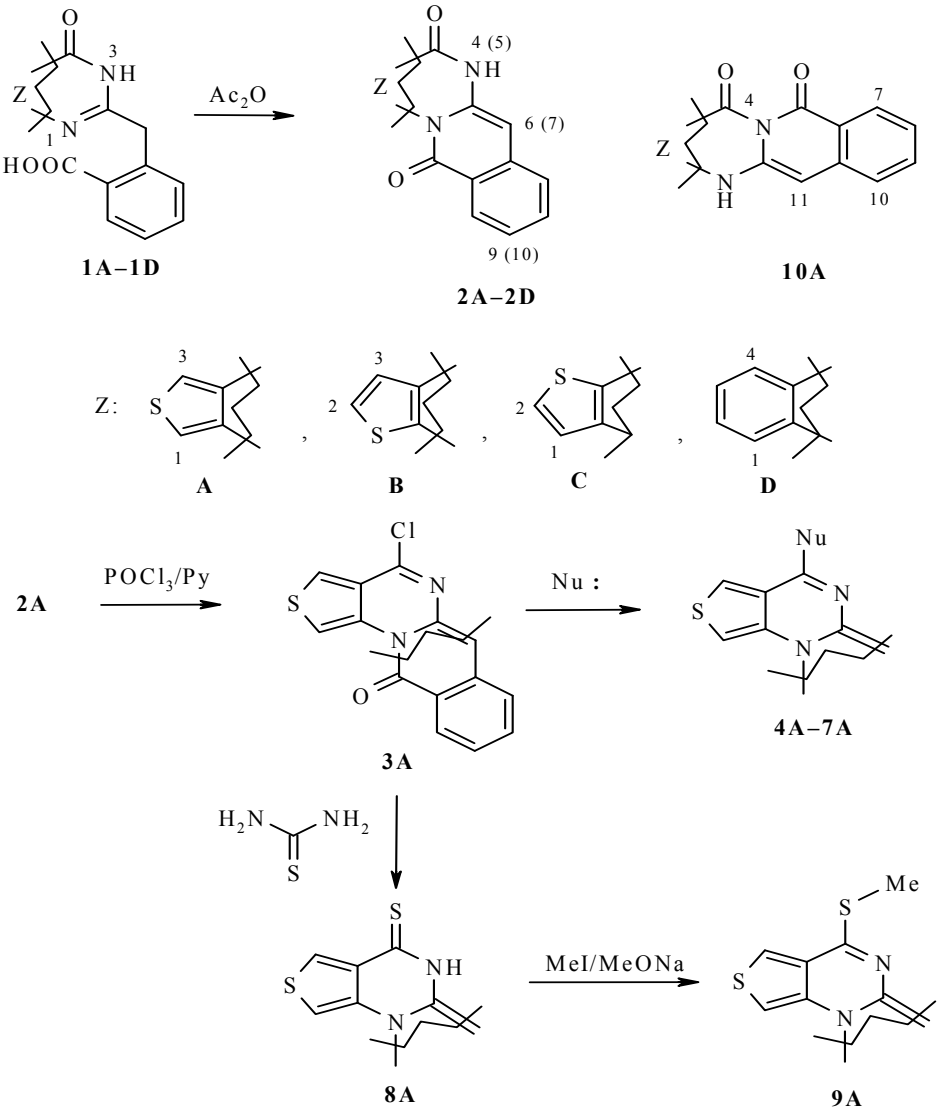
---

* For Communication 34, see [1].

** To whom correspondence should be addressed, e-mail: vkovtunenko@univ.kiev.ua, e-mail: shura_zd@ukr.net.

[1]Taras Shevchenko Kiev National University, Kiev 01033, Ukraine.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, 1185-1195, August, 2010. Original article submitted April 3, 2009. Revised version submitted May 13, 2010.



4A NuH = pyrrolidine, **5A** NuH = piperidine, **6A** NuH = morpholine, **7A** Nu: = methoxide anion

The numbering of the atoms in the Scheme, which is not always according to IUPAC rules, is used later to assign the proton signals in the ^{1}H NMR spectra (Table 2).

Analogous conclusions on the cyclization of acid **1A** at atom N(1) follow from analysis of data of two-dimensional spectra of homonuclear (COSY, NOESY) and heteronuclear ^{1}H-^{13}C correlation through a single bond (HMQC) and through 2-3 bonds (HMBC) for compound **2A** (Table 1).

Examination of the formulas of isomers **2A** and **10A** shows that in the case of the linear isomer **10A** it would be expected that the proton of the NH unit would be close to the aromatic protons H-1 and H-11, while in the case of the angular isomer **2A** it would be close to only one (H-6). In the NOESY spectrum there is only a cross peak between the signal of the proton of the NH unit and a signal at 6.27 ppm. No other cross peaks were observed for these protons, which is in complete accord with compound **2A**. Further confirmation of the structure of **2A** follows from the data on heteronuclear correlation shown in Table 1 and the Figure. The assignment of the chemical shifts of carbon atoms bonded to hydrogen atoms are based on the HMQC

correlation, while the assignment of the quaternary carbon atoms is based on the HMBC correlations. Most important from the point of view of establishing the structure are the absence of correlations between the signals of the proton of the NH unit and the ^{13}C atom with a chemical shift of 116.7 ppm, assigned to the atom $^{13}C(1)$ of the thiophene ring. In the alternative linear structure **10A** this correlation should be intense.

The correlations found permit the assignment of the remaining signals in complete agreement with the angular structure of **2A**.

It is of interest to examine the synthesized compound **2A** and its positional isomers **2B**, **2C**, and **2D**, prepared previously [5], from the point of view of how the position of the sulfur atom and the replacement of the thiophene ring by the benzene ring affect their physicochemical characteristics.

Comparison of the IR spectra of compounds **2A-2D** indicates that these transformations of the structure do not affect the positions of the carbonyl group absorption which is observed at 1664-1674 cm^{-1}.

Analysis of the ^{1}H NMR spectra (Table 2) permits the effect of some influence of changes in structure on the chemical shift of the NH proton: it is found at the weakest field (12.03) in the case of isomer **2C** and at the strongest field (11.39 ppm) in the case of isomer **2A**. The chemical shifts of the analogous proton of the isosteres **2B** and **2C** differ only slightly (11.71 and 11.87 ppm respectively).

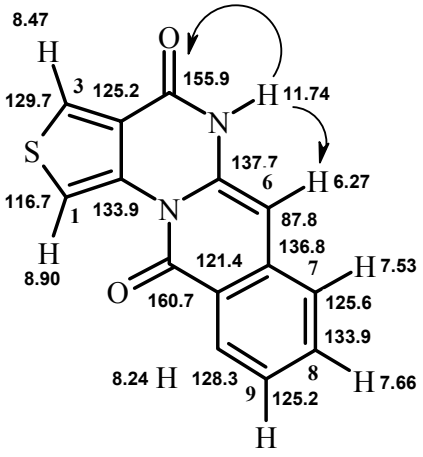


TABLE 1. Experimental Results for Homonuclear (NOESY) and Heteronuclear (HMBC and HMQC) Correlations for Compound **2A**

Position of atom (see Fig.)	^{1}H NMR spectrum, δ, ppm	HMQC	HMBC	NOESY
1	8.90	116.7	129.7, 125.2	—
3	8.47	129.7	155.9 (s), 133.9, 125.2, 116.7	—
5	11.74	—	155.9, 137.7, 129.7 (s), 125.2, 87.9	6.27
6	6.27	87.8	137.7, 133.9, 128.3 (s), 125.6, 121.4	7.53, 11.74
7	7.53	125.6	136.8 (s), 125.2, 121.4, 87.9	6.27, 7.66
8	7.66	133.9	136.8, 128.3	7.37, 7.53
9	7.37	125.2	133.9 (s), 125.6, 121.4	7.66, 8.24
10	8.24	128.3	160.7, 136.8, 133.9	7.37

TABLE 2. Table 2. ^{1}H NMR Spectra of the Compounds Synthesized (DMSO-d_6), δ, ppm (*J*, Hz)

Compound	H-1 (1H)	H-2/2-CH_3	H-3/3-CH_3	H-(4)*/4-R	H-5(6), 1H, s	H-6(7), 1H, s	H-7(8)	H-8(9)	H-9(10), 1H	H-10(11), 1H
1	2	3	4	5	6	7	8	9	10	11
2A	8.40 (d, ^4J = 3.5)	—	8.90 (1H, d, ^4J = 3.5)	—	11.39	6.31	7.52 (1H, d, ^3J = 8.0)	7.66 (1H, t, ^3J = 8.0)	7.37 (t, ^3J = 8.0)	8.28 (d, ^3J = 8.5)
2B	—	2.41 (3H, s)	2.36 (35H, s)	—	11.71	6.30	7.50 (1H, d, ^3J = 8.0)	7.62 (1H, t, ^3J = 7.6)	7.32 (t, ^3J = 7.6)	8.22 (d, ^3J = 8.4)
2C	8.68 (d, ^3J = 5.2)	8.17 (1H, d, ^3J = 5.2)	—	—	12.03	6.27	7.47 (1H, d, ^3J = 7.6)	7.65 (1H, t, ^3J = 8.0)	7.33 (t, ^3J = 8.0)	8.21 (d, ^3J = 8.0)
2D	9.24 (d, ^3J = 7.2)	7.74 (1H, t, ^3J = 6.8)	7.48 (2H, m)	8.10 (1H, d, ^3J = 6.0)	11.87	6.20	7.48 (2H, m)	7.63 (1H, t, ^3J = 5.6)	7.32 (t, ^3J = 5.6)	8.19 (d, ^3J = 6.4)
3A	8.92 (d, ^4J = 3.0)	—	8.34 (1H, d, ^4J = 3.0)	—	—	7.06	7.81 (2H, m)		7.62 (t, ^3J = 6.5)	8.42 (d, ^3J = 8.0)
3B	—	2.41 (3H, s)	2.37 (3H, s)	—	—	7.13	7.80 (1H, d, ^3J = 7.0)	7.87 (1H, t, ^3J = 7.5)	7.59 (t, ^3J = 7.0)	8.37 (d, ^3J = 7.0)
3C	8.83 (m)	8.23 (1H, m)	—	—	—	7.07	7.81 (2H, m)		7.57 (m)	8.38 (d, ^3J = 7.5)
4A	9.09 (s)	—	8.38 (1H, s)	3.88 (4H, m, NCH_2); 2.00 (4H, m, $NCH_2C\underline{H_2}$)	—	6.40	7.50 (1H, d, ^3J = 6.5)		7.57 (t, ^3J = 6.0)	7.26 (t, ^3J = 7.0)
4B	—	2.37 (3H, s)	2.34 (3H, s)	3.63 (4H, m, NCH_2); 1.84 (4H, m, $NCH_2C\underline{H_2}$)	—	6.64	7.62 (2H, m)		7.29 (m)	8.21 (d, ^3J = 8.5)

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11
4C	9.00 (d, ^3J = 6.0)	8.18 (1H, d, ^3J = 5.5)	—	3.85 (4H, m, NCH_2); 2.00 (4H, m, $NCH_2C\underline{H}_2$)	—	6.49	7.54 (1H, d, ^3J = 7.5)		7.59 (t, ^3J = 7.5)	7.24 (t, ^3J = 7.5)
5A	9.00 (d, ^4J = 3.0)	—	8.31 (1H, d, ^4J = 2.5)	3.78 (4H, m, NCH_2); 1.69 (6H, m, $NCH_2(C\underline{H}_2)_3$)	—	6.55	7.62 (2H, m)		7.34 (t, ^3J = 7.5)	8.26 (d, ^3J = 8.5)
5B	—	2.38 (3H, s)	2.37 (3H, s)	3.32 (4H, m, NCH_2); 1.68 (4H, m, $NCH_2C\underline{H}_2$); 1.62 (2H, m, $NCH_2CH_2C\underline{H}_2$)	—	6.79	7.69 (2H, m)		7.38 (t, ^3J = 7.5)	8.26 (d, ^3J = 8.0)
5C	8.90 (d, ^3J = 5.5)	8.14 (1H, d, ^3J = 5.5)	—	3.89 (4H, m, NCH_2); 1.67 (6H, m, $NCH_2(C\underline{H}_2)_3$)	—	6.56	7.61 (2H, m)		7.29 (t, ^3J = 7.5)	8.25 (d, ^3J = 8.0)
6A	9.02 (d, ^4J = 3.0)	—	8.42 (1H, d, ^4J = 3.5)	3.78 (8H, m, $N(CH_2)_2O(CH_2)_2$)	—	6.60	7.64 (2H, m)		7.37 (t, ^3J = 7.5)	8.28 (d, ^3J = 8.0)
6B	—	2.36 (6H, s)		3.77 (4H, m, $NC\underline{H}_2CH_2O$); 3.34 (4H, m, $NCH_2C\underline{H}_2O$);	—	6.82	7.70 (2H, m)		7.40 (t, ^3J = 8.0)	8.26 (d, ^3J = 8.5)
6C	8.92 (d, ^3J = 6.0)	8.14 (1H, d, ^3J = 5.5)	—	3.90 (4H, m, $NC\underline{H}_2CH_2O$); 3.78 (4H, m, $NCH_2C\underline{H}_2O$)	—	6.58	7.59 (1H, d, ^3J = 7.5)		7.63 (t, ^3J = 7.0)	7.31 (t, ^3J = 7.5)
7A	8.88 (s)	—	8.25 (1H, s)	4.05 (3H, s, OCH_3)	—	6.77	7.71 (2H, m)		7.47 (s)	8.32 (d, ^3J = 8.0)

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11
7B	—	2.32 (3H, s)	2.29 (3H, s)	4.02 (3H, s, OCH_3)	—	6.82	7.72 (2H, m)		7.44 (m)	8.27 (d, ^3J = 8.0)
7C	8.80 (m)	8.11 (1H, m)	—	4.07 (3H, s, OCH_3)	—	6.77	7.68 (2H, m)		7.43 (m)	8.32 (d, ^3J = 6.0)
8A	8.92 (d, ^4J = 3.5)	—	8.57 (1H, d, ^4J = 3.5)	—	13.30	6.60	7.62 (1H, d, ^3J = 8.5)	7.71 (1H, t, ^3J = 7.5)	7.45 (t, ^3J = 7.5)	8.28 (d, ^3J = 8.0)
8B	—	2.58 (3H, s)	2.33 (3H, s)	—	13.15	6.60	7.63 (1H, d, ^3J = 8.0)	7.71 (1H, t, ^3J = 8.0)	7.41 (t, ^3J = 7.5)	8.21 (d, ^3J = 7.5)
8C	8.71 (d, ^3J = 6.0)	8.20 (1H, d, ^3J = 5.5)	—	—	13.46	6.57	7.61 (1H, d, ^3J = 7.5)	7.70 (1H, t, ^3J = 7.5)	7.41 (t, ^3J = 8.0)	8.25 (d, ^3J = 8.0)
9A	8.95 (s)	—	8.26 (1H, s)	2.69 (3H, s, SCH_3)	—	6.98	7.79 (2H, m)		7.55 (t ,^3J = 7.0)	8.38 (d, ^3J = 8.5)
9B	—	2.33 (3H, s)	2.24 (3H, s)	2.53 (3H, s, SCH_3)	—	6.87	7.72 (2H, m)		7.44 (t, ^3J = 7.5)	8.24 (d, ^3J = 8.0)
9C	8.87 (d, ^3J = 5.0)	8.15 (1H, d, ^3J = 5.0)	—	2.71 (3H, s, SCH_3)	—	7.05	7.79 (2H, m)		7.51 (t, ^3J = 7.0)	8.36 (d, ^3J = 8.5)

* Here and futher across the positions of the protons in compound **2D** are shown in brackets.

The electronic spectra of compounds **2A-2D** show intense absorptions in the long wavelength UV and visible region, 300-420 nm. The differences in these four are the notable bathochromic shift of the long wavelength absorption maxima of compounds **2A** and **2B** (28 and 56 nm respectively) and the small shift in the case of the isostere **2C** (12 nm) relative to the analogous maximum of compound **2D** (Table 3).

Analysis of the effect of substituents in position 4 on the physicochemical characteristics of the synthesized compounds **3**, **4**, **7**, and **9** of series **A** (data from the ^{1}H NMR and IR spectra) showed that they are similar to those we described [1] for their analogs of the series **B** and **C**. However comparison of the electronic spectra of compounds **3**, **4**, **7**, and **9** of series **A**, **B**, and **C** shows a definite difference between them. For example, substitution of substituent OMe in compound **7A** by chlorine, SMe, and pyrrolidine causes an almost uniform bathochromic shift of the absorption bands ($\Delta\lambda \approx 30$ nm). In the case of derivatives of series **B** and **C** the influence of the various substituents on the shift is different [1]. For compounds **3**, **4**, **7,** and **9** of series **B** it increases in the series OMe < $N(CH_2)_4$ < SMe < Cl while for the analogs in series **C** the series is OMe < $N(CH_2)_4$ < Cl < SMe. So the change in the position of the sulfur atom in the thiophene ring and the replacement of the latter by a benzene ring substantially affects the electronic structure of the derivatives described. Data on the electronic spectra of 4-SMe-substituted **9A**, **9B**, and **9C** (positional isomers) confirms the earlier conclusion: relative to the absorption band of compound **9A** the absorption bands of compounds **9B** and **9C** are shifted by 15 and 35 nm respectively.

In order to elucidate the biological potential of compounds **2-9** of series **A** we produced an estimate of the spectra of their biological activity using the program PASS (Prediction of Activity Spectra for Substances) [8-10]. The results of the estimation of the spectra of the probable biological activity of the synthesized compounds: **2A, 4A-9A** – agonists of the dopamine receptor D_4, $p_a = 0.853$-0.892; **3A** – stimulator of serotonin receptors, $p_a = 0.858$, and agonist of dopamine receptor D_4 , $p_a = 0.878$.

On the basis of the set of active compounds and the use of many equations to estimate the surroundings of the atoms and comparison with calculated 2D descriptors with this set, which correspond to high activity or zero activity. The end result of the program is the probability of the appearance of compounds with activity (p_a) or inactivity (p_i) in fractions of units. For each of the compounds a spectrum of more than 3000 types of activity was calculated. Compounds **2A-9A** have $p_a > 0.8$ and $p_i < 0.2$.

A high level of activity is suggested for compounds **2-9** of series **A** relative to the dopamine receptor D_4 for which they act as agonists [11].

Table 3. UV Spectra of Compounds **2-4**, **7** and **9**

Com-pound	λ_{max}, nm (log ε)*
2A	333 (3.94), 374 (3.83), 389 (3.66)
2B	303 (4.56), 376 (3.80), 396 (3.83), 417 (3.71)
2C	310 (4.01), 336 (3.87), 353 (3.86), 373 (3.80)
2D	294 (4.28), 361 (3.84)
3A	381 (3.96), 399 (4.01), 422 (4.04), 447 (3.80)
4A	312 (4.29), 397 (4.23), 422 (4.24), 445 (4.09)
7A	348 (4.05), 363 (4.16), 380 (4.20), 400 (4.20), 421 (3.95)
9A	381 (4.28), 403 (4.40), 425 (4.38), 450 (4.09)
9B	309 (4.83), 327 (4.44), 404 (4.38), 438 (3.99), 465 (3.58)
9C	324 (4.28), 380 (4.43), 398 (4.43), 432 (4.17), 459 (4.08), 485 (3.78)

* Data for compounds **2B-D** are from [7], data for compounds **9B** and **C** are from [1].

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer Spectrum BX instrument (using a Pike NPVO attachment), UV spectra of $5 \cdot 10^{-5}$M solutions in DMF on a Perkin Elmer Lambda 20 UV-vis spectrophotometer. ^{1}H NMR spectra of DMSO-d_6 solutions with TMS as internal standard were recorded with a Bruker Avance DRX 500 (500 MHz) instrument. The individuality of the compounds obtained was confirmed using an Agilent 1100 chromato-mass spectrometer with an Agilent LC/MSD SL selective detector, with sample injection in a trifluoroacetic acid matrix and with EI ionization. Melting points were measured in Pyrex capillaries in a Thiele apparatus and subjected to correction.

4H-Thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinoline-4,11(5H)-dione (2A) was obtained by method [4] from acid **1A** and acetic anhydride. Mp 300-302°C (DMF). Yield 90%. IR spectrum, ν, cm^{-1}: 1664 (C=O), 1623 (C=C), 1565, 1510, 1365, 1151, 812 (C=C–H), 776, 749, 691. Mass spectrum, *m/z* 269 [M^++1]. Found, %: C 62.66; H 3.05; N 10.46; S 11.98. $C_{14}H_8N_2O_2S$. Calculated, %: C 62.68; H 3.01; N 10.44; S 11.95.

4-Chloro-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (3A) was obtained by method [7] from compound **2A** and phosphorus oxychloride. Mp 230-232°C (DMF). Yield 95%. IR spectrum, ν, cm^{-1}: 1661 (C=O), 1578 (C=N), 1548, 1479, 1297, 1232, 1077, 923, 799, 751 (C–Cl). Mass spectrum, *m/z* 287 [M^++1]. Found, %: C 58.68; H 2.48; Cl 12.31; N 9.79; S 11.23. $C_{14}H_7ClN_2OS$. Calculated, %: C 58.64; H 2.46; Cl 12.36; N 9.77; S 11.18.

4-Pyrrolidin-1-yl-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (4A) was obtained by method [7] from compound **3A** and pyrrolidine. Mp 220-222°C (EtOH). Yield 90%. IR spectrum, ν, cm^{-1}: 1641 (C=O), 1565 (C=N), 1530, 1335, 880, 800. Mass spectrum, *m/z*: 324 [M^++1]. Found, %: C 67.24; H 4.68; N 13.01; S 10.00. $C_{18}H_{15}N_3OS$. Calculated, %: C 67.27; H 4.70; N 13.07; S 9.98.

4-Piperidin-1-yl-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (5A) was obtained from compound **3A** and piperidine. Mp 160-162°C (EtOH). Yield 95%. IR spectrum, ν, cm^{-1}: 2932, 2851 (C–H), 1646 (C=O), 1613 (C=C), 1565 (C=N), 1535, 1280, 880, 794. Mass spectrum, *m/z* 338 [M^++1]. Found, %: C 68.02; H 5.08; N 12.52; S 10.00. $C_{19}H_{17}N_3OS$. Calculated, %: C 68.04; H 5.11; N 12.53; S 9.56.

4-Morpholin-4-yl-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (6A) was obtained by method [7], from compound **3A** and morpholine. Mp 180-182°C (EtOH). Yield 95%. IR spectrum, ν, cm^{-1}: 2851 (C–H), 1664 (C=O), 1618 (C=C), 1565 (C=N), 1540, 1482, 1450, 1267, 1113 (C–O), 1001, 880, 800, 749, 690. Mass spectrum, *m/z*: 338 [M^++1]. Found, %: C 64.00; H 4.45; N 12.41; S 9.54. $C_{18}H_{15}N_3O_2S$. Calculated, %: C 64.08; H 4.48; N 12.45; S 9.50.

4-Methoxy-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (7A) was obtained by method [7] from compound **3A** and sodium methoxide. Mp 190-192°C (DMF). Yield 90%. IR spectrum, ν, cm^{-1}: 1656 (C=O), 1593 (C=C), 1555 (C=N), 1487, 1328, 1306, 1105 (C–O), 812. Mass spectrum, *m/z*: 383 [M^++1]. Found, %: C 63.80; H 3.60; N 9.98; S 11.30. $C_{15}H_{10}N_2O_2S$. Calculated, %: C 63.82; H 3.57; N 9.92; S 11.36.

4-Thioxo-4,5-dihydro-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (8A) was obtained by method [7] from compound **3A** and thiourea. Mp 320-322°C (EtOH). Yield 95%. IR spectrum, ν, cm^{-1}: 1684 (C=O), 1625 (C=C), 1555, 1484, 1370, 1234 (C=S), 802, 736, 688. Found, %: C 59.10; H 2.80; N 9.82; S 22.50. $C_{14}H_8N_2OS_2$. Calculated, %: C 59.13; H 2.84; N 9.85; S 22.55.

4-Methylthio-11H-thieno[3',4':5,6]pyrimido[1,2-*b*]isoquinolin-11-one (9A) was obtained by method [7] from compound **8A** and methyl iodide. Mp 180-182°C (DMF). Yield 95%. IR spectrum, ν, cm^{-1}: 1651 (C=O), 1618 (C=C), 1537 (C=N), 1517, 1479, 1229, 935, 782, 738, 682 (C–S). Mass spectrum, *m/z*: 299 [M^++1]. Found, %: C 60.40; H 3.36; N 9.42; S 21.45. $C_{15}H_{10}N_2OS_2$. Calculated, %: C 60.38; H 3.38; N 9.39; S 21.49.

The authors thank the company "Enamin" (Kiev) for supporting this project.

REFERENCES

1. A. V. Zadorozhny and V. A. Kovtunenko, *Khim. Geterotsikl. Soedin.,* 619 (2009). [*Chem. Heterocycl. Comp.,* **45**, 489 (2009)].
2. A.V. Zadorozhny, A. V. Turov, and V. A. Kovtunenko, *Khim. Heterocycl. Soedin.,* 1227 (2010). [*Chem. Heterocycl. Comp.,* **46**, 991 (2010)].
3. T. T. Kucherenko, A. V. Zadorozhny, and V. A. Kovtunenko, *Khim. Geterotsikl. Soedin.,* 932 (2008). [*Chem. Heterocycl. Comp.,* **44**, 750 (2008)].
4. V. A Kovtunenko, T. T. Kucherenko, O. V. Shishkin, and V. M. Kisel', *Khim. Geterotsikl. Soedin.,* 1408 (2002). [*Chem. Heterocycl. Comp.,* **38**, 1242 (2002)].
5. A. V. Zadorozhny, V. A. Kovtunenko, A. V. Turov, and T. T. Kucherenko, *Khim. Geterotsikl. Soedin.,* 1053 (2008). [*Chem. Heterocycl. Comp.,* **44**, 845 (2008)].
6. HyperChem Professional 5.1, Hypercube © Inc, 2002. (Loaned by Prof. O. D. Kachkovskii (Institute of Organic Chemistry, Ukraine National Academy of Science, Kiev).
7. A. V. Zadorozhny, V. A. Kovtunenko, A. A. Viniichuk, and A. D. Kachkovskii, *Zh. Org. Farm. Khim,* **7,** Pt. 3(24), 64 (2009).
8. D. A. Filimonov, V. V. Poroikov, Yu. V. Borodina, and T. Gloriozova, *J. Chem. Inf. Comput, Sci.,* **39**, 666 (1999).
9. V. V. Poroikov, D. A. Filimonov, Yu. V. Borodina, A. A. Lagunin, and A. Kos, *J. Chem. Inf. Comput. Sci.* **40**, 1349 (2000).
10. V. V. Poroikov and D. A. Filimonov, *J. Comput. Aided Mol. Des.,* **16,** 819 (2002).
11. P. Seeman and S. List, in: *Abstracts of the 8th Symposium International Congr. Pharmacol., Okayama, July 1981,* Oxford, 1982, p. 61.