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Synthesis of 10-alkylsulfanyl-substituted pyrido-[4',3':4,5]thieno[3,2-*d*]pyrimidines annulated with pyran, cyclohexane, and cyclopentane rings

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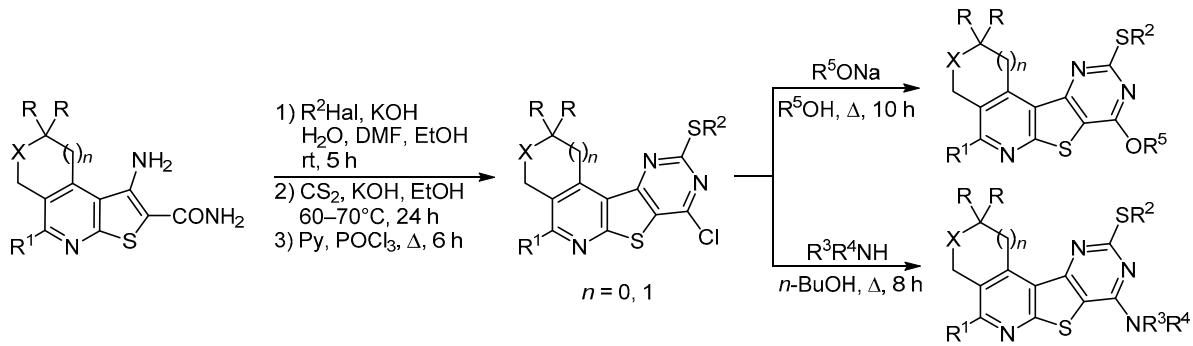


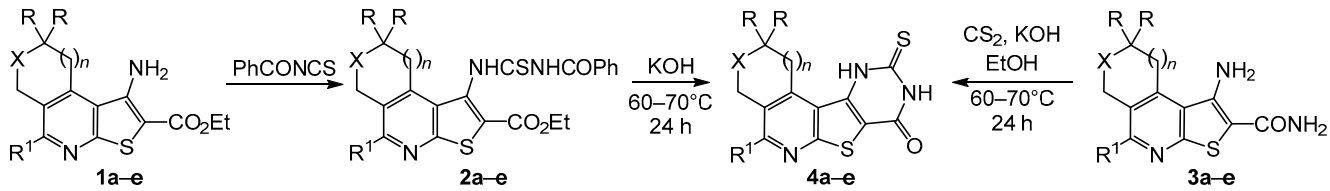
We propose a single-step procedure for the synthesis of 8-oxo-10-sulfanylpyrido[4',3':4,5]thieno[3,2-*d*]pyrimidines, annulated with pyran, cyclohexane, or cyclopentane rings. The alkylation of these compounds in aqueous DMF solution of KOH at room temperature was shown to proceed regioselectively and led to the formation of *S*-substituted products. Amino- and alkoxy-substituted derivatives of tetracyclic thieno[3,2-*d*]pyrimidines were synthesized. The antimicrobial activity of the obtained compounds was studied on Gram-positive staphylococci and Gram-negative rods.

Keywords: 10-alkylsulfanyl-8-oxothieno[3,2-*d*]pyrimidines, carbon disulfide, functionalized pyrimidines, antimicrobial activity, regioselectivity.

The pyrimidine ring is a part of many natural and synthetic compounds, while pyridine derivatives and condensed systems containing pyridine rings have anti-inflammatory, analgesic, and antibacterial properties.[1–4] The preparation of tricyclic pyrido[4',3':4,5]thieno[3,2-*d*]-pyrimidines from 3-amino-2-cyano(ethoxycarbonyl)thieno-[2,3-*b*]pyridines has been described in the literature, and these compounds show antitumor, antiviral, and antimicrobial effects.[5–12] The biological importance of condensed pyrimidine derivatives has motivated significant interest towards the synthesis of new pyrido[4',3':4,5]thieno[3,2-*d*]-pyrimidine derivatives annulated with pyran, cyclohexane, and cyclopentane rings.

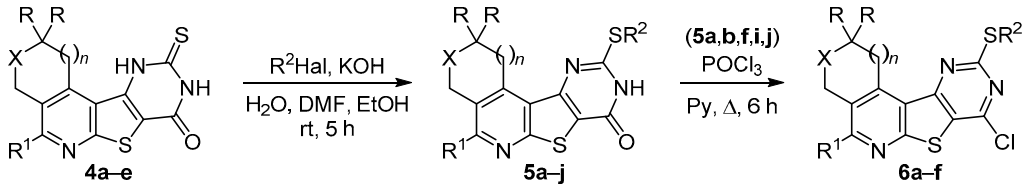
In this work, we continued the synthetic studies of functionalized tetracyclic thieno[3,2-*d*]pyrimidines by focusing on the methods for preparing derivatives of the respective heterocycles. Previously we have reported a two-stage method for the synthesis of 8-oxo-10-thioxothieno[3,2-*d*]-pyrimidines **4a**–**e**: in reactions of 1-amino-2-ethoxycarbonyl-thieno[2,3-*b*]pyridines **1a**–**e** with benzoylisothiocyanate, involving the formation of *N,N'*-disubstituted thioureas **2a**–**e** as intermediates, which were subsequently cyclized in the presence of alkali.[13] We also described a more efficient one-step procedure[14] for the synthesis of compounds **4b**,**d** by a reaction of 1-amino-2-carbamoylthieno[2,3-*b*]pyridines **3b**,**d** with carbon disulfide in the presence of pyridine. In that case, potassium hydroxide solution in ethanol was selected as base for the synthesis of compounds **4a**–**e** from aminoamides **3a**–**e**,[15] allowing to increase the yields of target products to 90–95% (Scheme 1).

Scheme 1



a X = O, *n* = 1, R = Me, R^1 = pyrrolidin-1-yl; **b** X = O, *n* = 1, R = Me, R^1 = morpholin-4-yl; **c** X = CH_2, *n* = 1, R = H, R^1 = pyrrolidin-1-yl
d X = CH_2, *n* = 1, R = H, R^1 = morpholin-4-yl; **e** X = CH_2, *n* = 0, R = H, R^1 = morpholin-4-yl

Scheme 2



5a, **6a** X = O, *n* = 1, R = Me, R^1 = pyrrolidin-1-yl, R^2 = Me; **5b–e**, **6c** X = O, *n* = 1, R = Me, R^1 = morpholin-4-yl
5f, **6d** X = CH_2, *n* = 1, R = H, R^1 = pyrrolidin-1-yl, R^2 = Me; **5g,h,i**, **6e** X = CH_2, *n* = 1, R = H, R^1 = morpholin-4-yl
5j, **6f** X = CH_2, *n* = 0, R = H, R^1 = morpholin-4-yl, R^2 = Me; **5b**, **6c** R^2 = Bn
5c R^2 = *n*-C_4H_9, **d** R^2 = $CH_2CONHPh$, **e** R^2 = $CH_2CH{=}CH_2$, **g** R^2 = Me, **h** R^2 = CH_2COPh; **5i**, **6e** R^2 = Bn

We found that alkylation of 8-oxo-10-thioxothieno[3,2-*d*]-pyrimidines **4a**–**e** in aqueous DMF solution of KOH at 20–22°C occurred regioselectively with the formation of *S*-alkyl derivatives **5a**–**j**. The regioselectivity of this reaction was explained by the greater polarizability of sulfur atom, compared to the nitrogen and oxygen atoms.[16] The signals of *S*-methyl and *S*-methylene group protons were observed in ^{1}H NMR spectra of compounds **5a**–**j** at the ranges of 2.60–2.62 and 3.22–4.90 ppm, respectively, while ^{13}C NMR signals of these groups were at 13.0–13.5 ppm (compounds **5a**,**f**,**g**,**j**) and 31.1–38.5 ppm (compounds **5b**–**e**,**h**,**i**), confirming the formation of *S*-alkylated products.[17]

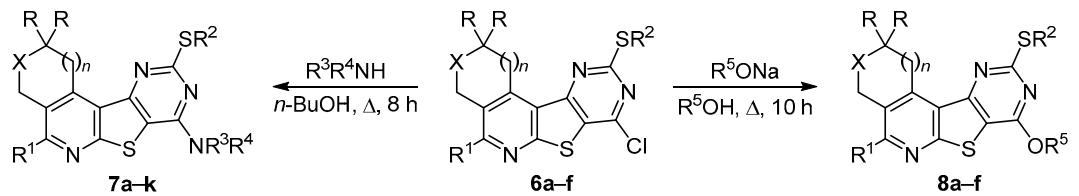
The treatment of *S*-alkyl derivatives **5a**,**b**,**f**,**i**,**j** with phosphorus oxychloride further gave 10-alkylsulfanyl-8-chlorothieno[3,2-*d*]pyrimidines **6a**,**c**–**f** (Scheme 2). The preparation of compound **6b** was described previously.[18]

The reactions of compounds **6a**–**f** with amines provided 5,8-diamino-substituted 10-alkylsulfanylthieno[3,2-*d*]pyrimidines **7a**–**k**, while treatment with sodium alkoxide in the appropriate alcohol gave the 8-alkoxy derivatives **8a**–**f** (Scheme 3). The signals of NH group in ^{1}H NMR spectra of compounds **7a**,**c**,**d**,**f**,**h** were observed in the range of 7.30–8.09 ppm, while the signals of OCH_3, OCH_2, and OCH groups in spectra of compounds **8a**–**f** were observed in the range of 4.16–5.61 ppm.

The antimicrobial activity of compounds **5a**–**j**, **7a**–**k**, and **8a**–**f** was studied by the agar diffusion assay.[19] 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 **5b**,**h**, **7a**,**d**,**e**,**h**, and **8c**,**d**,**f** had weak activity against all tested microbial strains: the diameters *d* of growth inhibition zones were 10–15 mm (Table 1). The indicated compounds were significantly less active than the reference drug furazolidone (*d* 24–25 mm).[20]

Thus, as a result of our studies, an efficient method has been developed for the preparation of 8-oxo-10-sulfanyl-pyrido[4',3':4,5]thieno[3,2-*d*]pyrimidines annulated with saturated rings, and 90–95% yields were achieved.

Scheme 3



7a,**b**, **8a** X = O, *n* = 1, R = R^2 = Me R^1 = pyrrolidin-1-yl; **7c**,**d**, **8b**,**c** X = O, *n* = 1, R = R^2 = Me, R^1 = morpholin-4-yl
7e,**f**, **8d** X = O, *n* = 1, R = Me, R^1 = morpholin-4-yl, R^2 = Bn; **7g**,**h**, **8e** X = CH_2, *n* = 1, R = H, R^1 = pyrrolidin-1-yl, R^2 = Me
7i, **8f** X = CH_2, *n* = 1, R = H, R^1 = morpholin-4-yl, R^2 = Bn; **7j**,**k** X = CH_2, *n* = 0, R = H, R^1 = morpholin-4-yl, R^2 = Me
7a R^3 = H, R^4 = 3-$PyCH_2$; **b**,**k** R^3R^4 = morpholin-4-yl; **c** R^3 = H, R^4 = $(CH_2)_2Ph$; **d** R^3 = H, R^4 = *n*-C_6H_{13}
e R^3 + R^4 = 4-methylpiperazin-1-yl; **f** R^3 = H, R^4 = Bn; **g** R^3 = Et, R^4 = *n*-C_4H_9; **h** R^3 = H, R^4 = 2-$FurCH_2$
i,**j** R^3 + R^4 = pyrrolidin-1-yl; **8a**,**d**,**e**,**f** R^5 = Et; **b** R^5 = Me,**c** R^5 = *i*-Pr

Table 1. The antimicrobial activity of compounds **5b**,**h**, **7a**,**d**,**e**,**h**, **8c**,**d**,**f** and furazolidone (diameter of growth inhibition zone, mm)

Compound	*S. aureus*		*S. dysenteriae flexneri* 6858	*E. coli* 0-55
	209p	1		
5b	11	10	11	13
5h	10	11	14	10
7a	12	14	13	12
7d	13	12	13	15
7e	10	12	13	14
7h	12	11	10	15
8c	13	10	15	14
8d	14	11	14	15
8f	10	13	11	14
Furazolidone	25	24	24	24

Reaction conditions were found for alkylation of the latter compounds with various alkyl halides, enabling good regioselectivity. Functionalized derivatives of condensed pyrido[4',3':4,5]thieno[3,2-*d*]pyrimidines were synthesized and biological activity of the obtained compounds was evaluated, allowing to identify compounds with antimicrobial effects on the bacterial strains *Staphylococcus aureus* 209p, JC-1, *Shigella dysenteriae flexneri* 6858, and *Escherichia coli* 0-55, opening possibilities for further search of potential antimicrobial agents among this type of compounds.

Experimental

IR spectra were recorded for Nujol mulls on a Nicolet Avatar 330 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were acquired on a Varian Mercury Vx 300 instrument (300 and 75 MHz, respectively) in DMSO-d_6, with TMS as internal standard. The assignment of ^{1}H and ^{13}C NMR signals was supported by DEPT, NOESY, and HMQC data when needed (mixing time 1 s). Elemental analysis of the C, H, N, and S content was performed on a Euro EA 3000 Elemental Analyzer. The content of chlorine was determined by the classic Pregl procedure. Melting points were determined on a Boetius micro hot stage. The aminoamides **3a**–**e** were synthesized according to a previously published procedure.[15]

Preparation of compounds 4a–e (General method). Compound **3a**–**e** (10 mmol) and carbon disulfide (20 ml, 0.33 mol) were added to a solution of KOH (1.68 g, 30 mmol) in EtOH (50 ml). The mixture was refluxed on a water bath at 60–70°C for 24 h. The solution was cooled, the excess of carbon disulfide was removed by distillation and the residue was acidified with dilute acetic acid solution. The obtained precipitate was filtered off, washed with water, and recrystallized from DMSO.

2,2-Dimethyl-5-(pyrrolidin-1-yl)-10-thioxo-1,4,10,11-tetrahydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidin-8(9*H*)-one (4a). Yield 5.41 g (92%), light-yellow crystals, mp > 360°C. IR spectrum, *ν*, cm^{-1}: 1260 (C=S), 1668 (CO), 3427 (2NH). ^{1}H NMR spectrum, δ, ppm: 1.35 (6H, s, 2CH$_3$); 1.92–2.00 (4H, m, 3,4-CH$_2$ pyrrolidine); 3.28 (2H, s, 1-CH$_2$); 3.57–3.65 (4H, m, N(CH$_2$)$_2$ pyrrolidine); 4.75 (2H, s, 4-CH$_2$); 11.04 (1H, br. s, NH); 12.44 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 25.0 (3,4-CH$_2$ pyrrolidine); 26.1 (2CH$_3$); 35.9 (1-CH$_2$); 49.5 (2,5-CH$_2$ pyrrolidine); 59.9 (4-CH$_2$); 68.6 (C-2); 108.9; 112.5; 114.2; 140.0; 140.1; 156.0; 156.1; 160.2 (C-8); 174.6 (C-10). Found, %: C 55.72; H 5.25; N 14.48; S 16.47. $C_{18}H_{20}N_4O_2S_2$. Calculated, %: C 55.65; H 5.19; N 14.42; S 16.51.

2,2-Dimethyl-5-(morpholin-4-yl)-10-thioxo-1,4,10,11-tetrahydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidin-8(9*H*)-one (4b). Yield 3.84 g (95%), light-yellow crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm: 1.35 (6H, s, 2CH$_3$); 3.18–3.27 (4H, m, N(CH$_2$)$_2$ morpholine); 3.37 (2H, s, 1-CH$_2$); 3.72–3.81 (4H, m, O(CH$_2$)$_2$ morpholine); 4.64 (2H, s, 4-CH$_2$); 11.25 (1H, br. s, NH); 12.59 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 26.1 (2CH$_3$); 35.8 (1-CH$_2$); 49.5 (3,5-CH$_2$ morpholine); 59.2 (4-CH$_2$); 66.0 (2,6-CH$_2$ morpholine); 69.5 (C-2); 108.4; 113.5; 118.9; 140.7; 143.3; 156.9; 157.2; 159.4 (C-8); 175.6 (C-10). Found, %: C 53.52; H 4.93; N 13.97; S 15.72. $C_{18}H_{20}N_4O_3S_2$. Calculated, %: C 53.45; H 4.98; N 13.85; S 15.85.

5-(Pyrrolidin-1-yl)-10-thioxo-1,2,3,4,10,11-hexahydro-pyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8(9*H*)-one (4c). Yield 3.26 g (91%), yellow crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66–1.77 (2H, m, 2-CH$_2$); 1.86–2.00 (6H, m, 3-CH$_2$, 3,4-CH$_2$ pyrrolidine); 2.71 (2H, br. t, *J* = 5.8, 4-CH$_2$); 3.35 (2H, br. t, *J* = 6.3, 1-CH$_2$); 3.58–3.65 (4H, m, N(CH$_2$)$_2$ pyrrolidine); 10.48 (1H, br. s, NH); 12.43 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 20.9 (2-CH$_2$); 22.0 (3-CH$_2$); 25.2 (3,4-CH$_2$ pyrrolidine); 26.0 (4-CH$_2$); 27.1 (1-CH$_2$); 49.8 (2,5-CH$_2$ pyrrolidine); 108.3; 113.0; 117.7; 140.3; 143.1; 156.3; 159.4; 159.5 (C-8); 174.3 (C-10). Found, %: C.88; H 5.12; N 15.72; S 17.76. $C_{17}H_{18}N_4OS_2$. Calculated, %: C 56.96; H 5.06; N 15.63; S 17.89.

5-(Morpholin-4-yl)-10-thioxo-1,2,3,4,10,11-hexahydro-pyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8(9*H*)-one (4d). Yield 3.41 g (91%), white crystals, mp 313–315°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.68–1.79 (2H, m, 2-CH$_2$); 1.87–2.00 (2H, m, 3-CH$_2$); 2.68 (2H, br. t, *J* = 5.9, 4-CH$_2$); 3.21–3.32 (4H, m, N(CH$_2$)$_2$ morpholine); 3.45 (2H, br. t, *J* = 6.7, 1-CH$_2$); 3.72–3.81 (4H, m, O(CH$_2$)$_2$ morpholine); 10.70 (1H, br. s, NH); 12.59 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 21.4 (2-CH$_2$); 22.0 (3-CH$_2$); 26.2 (4-CH$_2$); 26.8 (1-CH$_2$); 49.8 (3,5-CH$_2$ morpholine); 66.2 (2,6-CH$_2$ morpholine); 108.3; 113.1; 118.1; 141.3; 145.1; 154.3; 157.8; 159.2 (C-8); 174.8 (C-10). Found, %: C.61; H 4.90; N 14.88; S 17.21. $C_{17}H_{18}N_4O_2S_2$. Calculated, %: C 54.52; H 4.84; N 14.96; S 17.13.

4-(Morpholin-4-yl)-9-thioxo-2,3,9,10-tetrahydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7-(8*H*)-one (4e). Yield 3.24 g (90%), gray crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.08–2.20 (2H, m, 2-CH$_2$); 2.95 (2H, t, *J* = 7.2, 3-CH$_2$); 3.43 (2H, t, *J* = 7.3, 1-CH$_2$); 3.51–3.57 (4H, m, N(CH$_2$)$_2$ morpholine); 3.71–3.77 (4H, m, O(CH$_2$)$_2$ morpholine); 11.49 (1H, br. s, NH). 12.43 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 25.2

(2-CH_2); 29.2 (3-CH_2); 34.1 (1-CH_2); 47.9 (3,5-CH_2 morpholine); 66.3 (2,6-CH_2 morpholine); 108.6; 112.1; 115.2; 139.8; 140.0; 156.1; 156.3; 159.6 (C-7); 178.4 (C-9). Found, %: C 53.40; H 4.53; N 15.46; S 17.68. $C_{16}H_{16}N_4O_2S_2$. Calculated, %: C 53.31; H 4.47; N 15.54; S 17.79.

Preparation of compounds 5a–j (General method). DMF (25 ml) and compound **4a–e** (5 mmol) were added to a solution of KOH (0.28 g, 5 mmol) in water (2.5 ml). The mixture was treated by dropwise addition of the appropriate alkyl halide (5 mmol) solution in ethanol (15 ml). The mixture was stirred for 5 h at room temperature. The obtained crystals were filtered off and recrystallized from 2:1 mixture of EtOH and DMF.

2,2-Dimethyl-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido-[3',2':4,5]-thieno[3,2-*d*]pyrimidin-8(9*H*)-one (5a). Yield 1.95 g (97%), white crystals, mp > 360°C. IR spectrum, *ν*, cm^{-1}: 1652 (CO), 3420 (NH). ^{1}H NMR spectrum, δ, ppm: 1.30 (6H, s, $2CH_3$); 1.84–1.91 (4H, m, 3,4-CH_2 pyrrolidine); 2.60 (3H, s, SCH_3); 3.35 (2H, s, 1-CH_2); 3.56–3.62 (4H, m, $N(CH_2)_2$ pyrrolidine); 4.81 (2H, s, 4-CH_2); 12.85 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 13.1 (SCH_3); 25.1 ($2CH_3$); 26.4 (3,4-CH_2 pyrrolidine); 37.8 (1-CH_2); 49.6 (2,5-CH_2 pyrrolidine); 60.1 (4-CH_2); 68.7 (C-2); 114.8; 116.4; 141.4; 152.4; 152.5; 156.3; 157.6; 158.2 (C-8); 160.0 (C-10). Found, %: C 56.76; H 5.56; N 13.83; S 15.81. $C_{19}H_{22}N_4O_2S_2$. Calculated, %: C 56.69; H 5.51; N 13.92; S 15.93.

10-Benzylsulfanyl-2,2-dimethyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno-[3,2-*d*]pyrimidin-8(9*H*)-one (5b). Yield 2.25 g (98%), white crystals, mp 314–315°C. ^{1}H NMR spectrum, δ, ppm: 1.17 (6H, s, $2CH_3$); 3.15–3.21 (4H, m, $N(CH_2)_2$ morpholine); 3.34 (2H, s, 1-CH_2); 3.72–3.76 (4H, m, $O(CH_2)_2$ morpholine); 4.59 (2H, s, SCH_2); 4.65 (2H, s, 4-CH_2); 7.23–7.36 (3H, m, H Ph); 7.43–7.47 (2H, m, H Ph); 13.10 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 26.6 ($2CH_3$); 33.8 (SCH_2); 37.0 (1-CH_2); 49.9 (3,5-CH_2 morpholine); 59.2 (4-CH_2); 66.1 (2,6-CH_2 morpholine); 69.3 (C-2); 119.4; 119.8; 127.2 (C-4 Ph); 128.3 (C-3,5 Ph); 128.4 (C-2,6 Ph); 136.9 (C-1 Ph); 142.9; 151.8; 157.8; 157.9; 158.0; 158.9 (C-8); 159.1 (C-10). Found, %: C 60.62; H 5.35; N 11.22; S 13.10. $C_{25}H_{26}N_4O_3S_2$. Calculated, %: C 60.71; H 5.30; N 11.33; S 12.97.

10-Butylsulfanyl-2,2-dimethyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidin-8(9*H*)-one (5c). Yield 2.25 g (98%), white crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.92 (3H, t, *J* = 7.3, $CH_2C\underline{H}_3$); 1.30 (6H, s, $2CH_3$); 1.39–1.51 (2H, m, $SCH_2C\underline{H}_2$); 1.67–1.77 (2H, m, $C\underline{H}_2CH_3$); 3.16–3.21 (4H, m, $N(CH_2)_2$ morpholine); 3.22 (2H, t, *J* = 7.4, SCH_2); 3.41 (2H, s, 1-CH_2); 3.72–3.77 (4H, m, $O(CH_2)_2$ morpholine); 4.68 (2H, s, 4-CH_2); 12.99 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 13.5 ($CH_2\underline{C}H_3$); 21.6 (CH_2); 26.8 ($2CH_3$); 29.9 (CH_2); 31.1 (SCH_2); 37.0 (1-CH_2); 49.9 (3,5-CH_2 morpholine); 59.2 (4-CH_2); 66.1 (2,6-CH_2 morpholine); 69.4 (C-2); 115.0; 117.9; 119.4; 119.8; 142.8; 157.8; 158.3; 158.9 (C-8); 159.1 (C-10). Found, %: C 57.46; H 6.17; N 12.04; S 13.81. $C_{22}H_{28}N_4O_3S_2$. Calculated, %: C 57.37; H 6.13; N 12.16; S 13.92.

2-{[2,2-Dimethyl-5-(morpholin-4-yl)-8-oxo-1,4,8,9-tetrahydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidin-10-yl]sulfanyl}-*N*-phenylacetamide (5d). Yield 2.58 g (96%), light-yellow crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm: 1.13 (6H, s, $2CH_3$); 3.12–3.20 (4H, m, $N(CH_2)_2$ morpholine); 3.67–3.76 (4H, m, $O(CH_2)_2$ morpholine); 3.31 (2H, s, 1-CH_2); 4.23 (2H, s, SCH_2); 4.60 (2H, s, 4-CH_2); 6.99–7.06 (1H, m, H Ph); 7.24–7.32 (2H, m, H Ph); 7.52–7.58 (2H, m, H Ph); 10.19 (1H, br. s, NH); 13.14 (1H, br. s, 9-NH). ^{13}C NMR spectrum, δ, ppm: 26.5 ($2CH_3$); 36.8 (SCH_2); 38.7 (1-CH_2); 49.8 (3,5-CH_2 morpholine); 59.0 (4-CH_2); 66.0 (2,6-CH_2 morpholine); 69.5 (C-2); 119.1 (C-3,5 Ph); 119.5; 119.8; 123.3 (C-4 Ph); 128.7 (C-2,6 Ph); 138.8 (C-1 Ph); 138.9; 143.1; 152.0; 157.7; 158.8; 158.9 (C-8); 159.1 (C-10); 164.8 ($CH_2\underline{C}O$). Found, %: C 58.16; H 5.10; N 13.15; S 12.10. $C_{26}H_{27}N_5O_4S_2$. Calculated, %: C 58.08; H 5.06; N 13.03; S 11.93.

10-Allylsulfanyl-2,2-dimethyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidin-8(9*H*)-one (5e). Yield 2.09 g (94%), white crystals, mp 288–290°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.31 (6H, s, $2CH_3$); 3.17–3.25 (4H, m, $N(CH_2)_2$ morpholine); 3.43 (2H, s, 1-CH_2); 3.74–3.81 (4H, m, $O(CH_2)_2$ morpholine); 3.88 (2H, dt, *J* = 6.6, *J* = 1.2, SCH_2); 4.67 (2H, s, 4-CH_2); 5.15 (1H, dq, *J*=.0, *J* = 1.2) and 5.34 (1H, dq, *J* = 17.0, *J* = 1.2, CH=C$\underline{H}_2$); 6.04 (1H, ddt, *J* = 17.0, *J* = 10.0, *J* = 6.6, C$\underline{H}$=CH_2); 12.75 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 26.4 ($2CH_3$); 32.6 (SCH_2); 37.0 (1-CH_2); 49.9 (3,5-CH_2 morpholine); 59.2 (4-CH_2); 66.0 (2,6-CH_2 morpholine); 69.0 (C-2); 117.2 (CH=C$\underline{H}_2$); 118.8; 120.2; 132.8 (C$\underline{H}$=CH_2); 141.2; 142.3; 151.4; 156.9; 157.8; 158.6 (C-8); 159.4 (C-10). Found, %: C 56.62; H 5.49; N 12.71; S 14.34. $C_{21}H_{24}N_4O_3S_2$. Calculated, %: C 56.73; H 5.44; N 12.60; S 14.43.

10-Methylsulfanyl-5-(pyrrolidin-1-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8(9*H*)-one (5f). Yield 1.73 g (93%), light-yellow crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm: 1.61–1.72 (2H, m, 2-CH_2); 1.76–1.93 (6H, m, 3,4-CH_2 pyrrolidine, 3-CH_2); 2.60 (3H, s, SCH_3); 2.67–2.74 (2H, m, 4-CH_2); 3.39–3.47 (2H, m, 1-CH_2); 3.53–3.61 (4H, m, $N(CH_2)_2$ pyrrolidine); 12.81 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 13.0 (SCH_3); 22.1 (2-CH_2); 25.1 (3,4-CH_2 pyrrolidine); 25.4 (3-CH_2); 26.0 (4-CH_2); 26.8 (1-CH_2); 49.7 (2,5-CH_2 pyrrolidine); 113.7; 115.4; 141.2; 151.8; 152.3; 155.6; 157.4; 158.5 (C-8); 161.0 (C-10). Found, %: C 58.13; H 5.45; N 14.92; S 17.14. $C_{18}H_{20}N_4OS_2$. Calculated, %: C 58.04; H 5.41; N 15.04; S 17.22.

10-Methylsulfanyl-5-(morpholin-4-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8(9*H*)-one (5g). Yield 1.85 g (95%), white crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm: 1.70–1.80 (2H, m, 2-CH_2); 1.85–1.96 (2H, m, 3-CH_2); 2.62 (3H, s, SCH_3); 2.68–2.74 (2H, m, 4-CH_2); 3.19–3.24 (4H, m, $N(CH_2)_2$ morpholine); 3.75–3.80 (4H, m, $O(CH_2)_2$ morpholine); 3.51–3.57 (2H, m,

1-CH_2); 12.85 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 13.0 (SCH_3); 20.8 (2-CH_2); 21.9 (3-CH_2); 26.0 (4-CH_2); 26.7 (1-CH_2); 49.6 (3,5-CH_2 morpholine); 65.7 (2,6-CH_2 morpholine); 113.2; 115.7; 141.4; 152.1; 153.5; 156.4; 157.6; 158.2 (C-8); 160.5 (C-10). Found, %: C 55.73; H 5.15; N 14.33; S 16.41. $C_{18}H_{20}N_4O_2S_2$. Calculated, %: C 55.65; H 5.19; N 14.42; S 16.51.

5-(Morpholin-4-yl)-10-[(2-oxo-2-phenylethyl)sulfanyl]-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]-isoquinolin-8(9*H*)-one (5h). Yield 2.29 g (93%), white crystals, mp 274–275°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.18–1.27 (2H, m, 2-CH_2); 1.49–1.58 (2H, m, 3-CH_2); 2.57 (2H, t, *J* = 5.9, 4-CH_2); 3.09 (2H, t, *J* = 6.4, 1-CH_2); 3.14–3.21 (4H, m, N(CH_2)$_2$ morpholine); 3.71–3.78 (4H, m, O(CH_2)$_2$ morpholine); 4.90 (2H, s, SCH_2); 7.52–7.58 (2H, m, H Ph); 7.61–7.68 (1H, m, H Ph); 8.05–8.11 (2H, m, H Ph); 12.97 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 20.9 (2-CH_2); 21.8 (3-CH_2); 25.8 (4-CH_2); 26.8 (1-CH_2); 38.5 (SCH_2); 49.5 (3,5-CH_2 morpholine); 65.9 (2,6-CH_2 morpholine); 115.6; 120.4; 121.4; 127.8 (C-3,5 Ph); 128.2 (C-2,6 Ph); 132.8 (C-4 Ph); 135.4 (C-1 Ph); 145.5; 151.7; 156.3; 157.6; 158.4 (C-8); 160.9 (C-10); 190.4 (CH_2CO). Found, %: C 60.87; H 4.96; N.49; S 13.10. $C_{25}H_{24}N_4O_3S_2$. Calculated, %: C 60.95; H 4.91; N 11.37; S 13.02.

10-Benzylsulfanyl-5-(morpholin-4-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8(9*H*)-one (5i). Yield 2.21 g (95%), white crystals, mp 325–327°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.61–1.84 (4H, m, 2,3-CH_2); 2.67 (2H, t, *J* = 5.3, 4-CH_2); 3.16–3.22 (4H, m, N(CH_2)$_2$ morpholine); 3.40 (2H, t, *J* = 5.8, 1-CH_2); 3.72–3.79 (4H, m, O(CH_2)$_2$ morpholine); 4.55 (2H, s, SCH_2); 7.23–7.38 (3H, m, H Ph); 7.43–7.47 (2H, m, H); 13.06 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 21.5 (2-CH_2); 22.0 (3-CH_2); 26.0 (4-CH_2); 26.9 (1-CH_2); 34.0 (SCH_2); 49.7 (3,5-CH_2 morpholine); 66.1 (2,6-CH_2 morpholine); 120.3; 122.3; 127.2 (C-4 Ph); 128.4 (C-3,5 Ph); 128.5 (C-2,6 Ph); 136.7 (C-1 Ph); 146.2; 152.1; 155.5; 157.4; 157.8; 158.2 (C-8); 161.5 (C-10). Found, %: C 61.95; H 5.26; N 12.18; S 13.71. $C_{24}H_{24}N_4O_2S_2$. Calculated, %: C 62.04; H 5.21; N 12.06; S 13.80.

9-Methylsulfanyl-4-(morpholin-4-yl)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-7(8*H*)-one (5j). Yield 1.80 g (96%), white crystals, mp > 360°C. ^{1}H NMR spectrum, δ, ppm (*J*,Hz): 2.06–2.16 (2H, m, 2-CH_2); 2.60 (3H, s, SCH_3); 2.95 (2H, t, *J* = 7.2, 3-CH_2); 3.34 (2H, t, *J* = 7.5, 1-CH_2); 3.47–3.53 (4H, m, N(CH_2)$_2$ morpholine); 3.70–3.76 (4H, m, O(CH_2)$_2$ morpholine); 12.87 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 25.1 (2-CH_2); 30.5 (3-CH_2); 30.9 (1-CH_2); 47.9 (3,5-CH_2 morpholine); 66.1 (2,6-CH_2 morpholine); 113.2; 117.5; 140.2; 151.9; 154.3; 155.6; 156.7; 158.6 (C-7); 163.6 (C-9). Found, %: C 54.61; H 4.79; N 14.87; S 17.02. $C_{17}H_{18}N_4O_2S_2$. Calculated, %: C 54.52; H 4.84; N 14.96; S 17.13.

Preparation of compounds 6a,c–f (General method). A mixture of compound **5a**,**b**,**f**,**i**,**j** (5 mmol), phosphorus oxychloride (25 ml, 0.268 mol), and pyridine (1.3 ml, 16 mmol) was refluxed for 6 h. The excess of phosphorus oxychloride was removed by distillation, the residue was quenched with ice water (50 ml) and neutralized with aqueous ammonia solution. The obtained crystals were filtered off, washed with water, and recrystallized from a 4:1 mixture of $CHCl_3$ and EtOH.

8-Chloro-2,2-dimethyl-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine (6a). Yield 1.71 g (81%), light-yellow crystals, mp 224–226°C. ^{1}H NMR spectrum, δ, ppm: 1.35 (6H, s, 2CH_3); 1.96–2.02 (4H, m, 3,4-CH_2 pyrrolidine); 2.60 (3H, s, SCH_3); 3.36 (2H, s, 1-CH_2); 3.66–3.73 (4H, m, N(CH_2)$_2$ pyrrolidine); 4.84 (2H, s, 4-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.8 (SCH_3); 25.1 (3,4-CH_2 pyrrolidine); 27.6 (2CH_3); 36.5 (1-CH_2); 50.1 (2,5-CH_2 pyrrolidine); 60.3 (4-CH_2); 68.6 (C-2); 115.6; 118.4; 121.5; 144.9; 151.7; 159.2; 160.5; 160.4 (C-8); 165.2 (C-10). Found, %: C 54.30; H 5.09; N 13.15; S 15.33; Cl 8.51. $C_{19}H_{21}ClN_4OS_2$. Calculated, %: C 54.21; H 5.03; N 13.31; S 15.23; Cl 8.42.

8-Chloro-2,2-dimethyl-10-methylsulfanyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidine (6b).[18] White crystals, mp 261–262°C. ^{1}H NMR spectrum, δ, ppm: 1.34 (6H, s, 2CH_3); 2.53 (3H, s, SCH_3); 3.16–3.27 (4H, m, N(CH_2)$_2$ morpholine); 3.51 (2H, s, 1-CH_2); 3.73–3.81 (4H, m, O(CH_2)$_2$ morpholine); 4.64 (2H, s, 4-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.6 (SCH_3); 27.3 (2CH_3); 36.9 (1-CH_2); 48.4 (3,5-CH_2 morpholine); 60.2 (4-CH_2); 66.9 (2,6-CH_2 morpholine); 68.4 (C-2); 115.7; 118.0; 121.7; 145.4; 151.7; 159.3; 160.6; 161.0 (C-8); 165.2 (C-10). Found, %: C 52.45; H 4.56; N 12.74; S 14.56. $C_{19}H_{21}ClN_4O_2S_2$. Calculated, %: C 52.23; H 4.84; N 12.82; S 14.67.

10-Benzylsulfanyl-8-chloro-2,2-dimethyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidine (6c). Yield 1.90 g (74%), white crystals, mp 247–248°C. ^{1}H NMR spectrum, δ, ppm: 1.27 (6H, s, 2CH_3); 3.28–3.37 (4H, m, N(CH_2)$_2$ morpholine); 3.34 (2H, s, 1-CH_2); 3.75–3.82 (4H, m, O(CH_2)$_2$ morpholine); 4.50 (2H, s, SCH_2); 4.64 (2H, s, 4-CH_2); 7.18–7.32 (3H, m, H Ph); 7.40–7.46 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 27.4 (2CH_3); 34.1 (SCH_2); 36.2 (1-CH_2); 47.8 (3,5-CH_2 morpholine); 60.1 (4-CH_2); 66.8 (2,6-CH_2 morpholine); 69.9 (C-2); 116.4; 119.7; 126.5 (C-4 Ph); 128.3 (C-3,5 Ph); 129.1 (C-2,6 Ph); 138.4 (C-1 Ph); 145.9; 151.4; 157.9; 158.2; 159.7; 160.4 (C-8); 165.1 (C-10). Found, %: C 58.40; H 4.96; N 10.84; S 12.58; Cl 6.83. $C_{25}H_{25}ClN_4O_2S_2$. Calculated, %: C 58.52; H 4.91; N 10.92; S 12.50; Cl 6.91.

8-Chloro-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinoline (6d). Yield 1.51 g (77%), yellow crystals, mp 216–217°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.71–1.79 (2H, m, 2-CH_2); 1.86–1.94 (2H, m, 3-CH_2); 1.95–2.01 (4H, m, 3,4-CH_2 pyrrolidine); 2.61 (3H, s, SCH_3); 2.77 (2H, br. t, *J* = 5.9, 4-CH_2); 3.48 (2H, br. t, *J* = 6.4, 1-CH_2); 3.65–3.72 (4H, m, N(CH_2)$_2$ pyrrolidine). ^{13}C NMR spectrum, δ, ppm: 13.9 (SCH_3); 21.1 (2-CH_2); 22.2 (3-CH_2); 25.1 (3,4-CH_2 pyrrolidine); 27.1 (4-CH_2); 27.4 (1-CH_2); 50.0 (2,5-CH_2 pyrrolidine); 115.1; 117.6; 121.1; 145.9; 151.4; 158.9;

160.3; 160.7 (C-8); 167.0 (C-10). Found, %: C 55.38; H 4.96; N 14.22; S 16.52; Cl 9.16. $C_{18}H_{19}ClN_4S_2$. Calculated, %: C 55.30; H 4.90; N 14.33; S 16.40; Cl 9.07.

10-Benzylsulfanyl-8-chloro-5-(morpholin-4-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinoline (6e). Yield 1.79 g (74%), light-yellow crystals, mp 246–248°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.72–1.78 (2H, m, 2-CH_2); 1.87–1.96 (2H, m, 3-CH_2); 2.74 (2H, t, *J* = 5.8, 4-CH_2); 3.25–3.34 (4H, m, N(CH_2)$_2$ morpholine); 3.51 (2H, t, *J* = 6.3, 1-CH_2); 3.77–3.85 (4H, m, O(CH_2)$_2$ morpholine); 4.52 (2H, s, SCH_2); 7.13–7.22 (3H, m, H Ph); 7.43–7.51 (2H, m, H Ph). ^{13}C NMR spectrum.: 21.2 (2-CH_2); 22.1 (3-CH_2); 26.9 (4-CH_2); 27.2 (1-CH_2); 34.0 (SCH_2); 47.9 (3,5-CH_2 morpholine); 66.7 (2,6-CH_2 morpholine); 121.6; 121.8; 126.8 (C-4 Ph); 128.5 (C-3,5 Ph); 128.8 (C-2,6 Ph); 138.2 (C-1 Ph); 145.6; 151.8; 158.0; 158.4; 159.5; 160.1 (C-8); 164.7 (C-10). Found, %: C 59.78; H 4.84; N 11.71; S 13.17; Cl 7.25. $C_{24}H_{23}ClN_4OS_2$. Calculated, %: C 59.67; H 4.80; N 11.60; S 13.28; Cl 7.34.

7-Chloro-9-methylsulfanyl-4-(morpholin-4-yl)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]-pyrimidine (6f). Yield 1.63 g (83%), white crystals, mp 250–251°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.16–2.26 (2H, m, 2-CH_2); 2.62 (3H, s, SCH_3); 3.03 (2H, t, *J* = 7.3, 3-CH_2); 3.43 (2H, t, *J* = 7.6, 1-CH_2); 3.63–3.70 (4H, m, N(CH_2)$_2$ morpholine); 3.73–3.80 (4H, m, O(CH_2)$_2$ morpholine). ^{13}C NMR spectrum, δ, ppm: 13.9 (SCH_3); 24.6 (2-CH_2); 27.8 (3-CH_2); 28.9 (1-CH_2); 47.8 (3,5-CH_2 morpholine); 66.4 (2,6-CH_2 morpholine); 114.6; 117.8; 125.3; 146.4; 151.6; 159.2; 160.5; 160.8 (C-7); 166.7 (C-9). Found, %: C 52.03; H 4.40; N 14.34; S 16.21; Cl 9.13. $C_{17}H_{17}ClN_4OS_2$. Calculated, %: C 51.96; H 4.36; N 14.26; S 16.32; Cl 9.02.

Preparation of compounds 7a–k (General method). Compound **6a**–**f** (3 mmol) in *n*-BuOH (40 ml) was treated with the appropriate amine (12 mmol). The mixture was refluxed for 8 h. The crystals that formed after cooling were filtered off, washed with water, ethanol, and recrystallized from a 1:1 mixture of $CHCl_3$ and EtOH.

2,2-Dimethyl-10-methylsulfanyl-*N*-(pyridin-3-ylmethyl)-5-(pyrrolidin-1-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-8-amine (7a). Yield 1.20 g (81%), light-yellow crystals, mp 211–212°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.34 (6H, s, 2CH_3); 1.93–2.01 (4H, m, 3,4-CH_2 pyrrolidine); 2.49 (3H, s, SCH_3); 3.45 (2H, s, 1-CH_2); 3.59–3.65 (4H, m, N(CH_2)$_2$ pyrrolidine); 4.73 (2H, d, *J*=.9, NHC$\underline{H}_2$); 4.77 (2H, s, 4-CH_2); 7.25 (1H, dd, *J* = 7.7, *J* = 4.8, H-5 Py); 7.77 (1H, ddd, *J* = 7.7, *J* = 1.9, *J* = 1.6, H-4 Py); 7.87 (1H, br. t, *J* = 5.9, NH); 8.40 (1H, dd, *J* = 4.8, *J* = 1.6, H-6 Py); 8.58 (1H, d, *J* = 1.9, H-2 Py). ^{13}C NMR spectrum, δ, ppm: 13.4 (SCH_3); 25.0 (3,4-CH_2 pyrrolidine); 26.3 (2CH_3); 37.3 (1-CH_2); 41.1 (NHCH_2); 49.5 (2,5-CH_2 pyrrolidine); 60.1 (4-CH_2); 68.5 (C-2); 105.9; 113.9; 116.2; 122.8 (C-4(5) Py); 135.2 (C-3 Py); 135.6 (C-5(4) Py); 141.6; 146.7 and 148.3 (C-2,6 Py); 155.4; 155.5; 156.3; 159.3 (C-8), 166.1 (C-10). Found, %: C60.83; H 5.79; N 17.19; S 13.10. $C_{25}H_{28}N_6OS_2$. Calculated, %: C 60.95; H 5.73; N 17.06; S 13.02.

2,2-Dimethyl-10-methylsulfanyl-8-(morpholin-4-yl)-5-(pyrrolidin-1-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (7b). Yield 1.10 g (78%), light-yellow crystals, mp 215–216°C. ^{1}H NMR spectrum, δ, ppm: 1.34 (6H, s, 2CH_3); 1.91–2.03 (4H, m, 3,4-CH_2 pyrrolidine); 2.53 (3H, s, SCH_3); 3.46 (2H, s, 1-CH_2); 3.59–3.64 (4H, m, N(CH_2)$_2$ pyrrolidine); 3.74–3.80 (4H, m, N(CH_2)$_2$ morpholine); 3.84–3.90 (4H, m, O(CH_2)$_2$ morpholine); 4.79 (2H, s, 4-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 25.1 (3,4-CH_2 pyrrolidine); 26.5 (2CH_3); 37.0 (1-CH_2); 48.6 (3,5-CH_2 morpholine); 49.7 (2,5-CH_2 pyrrolidine); 59.8 (4-CH_2); 66.5 (2,6-CH_2 morpholine); 68.9 (C-2); 107.8; 115.6; 118.4; 142.1; 154.7; 156.5; 157.2; 158.4 (C-8), 165.8 (C-10). Found, %: C 58.64; H 6.25; N 14.78; S 13.49. $C_{23}H_{29}N_5O_2S_2$. Calculated, %: C 58.57; H 6.20; N 14.85; S 13.60.

2,2-Dimethyl-10-methylsulfanyl-5-(morpholin-4-yl)-*N*-(2-phenylethyl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-8-amine (7c). Yield 1.30 g (83 %), white crystals, mp 189–190°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, s, 2CH_3); 2.56 (3H, s, SCH_3); 2.99 (2H, t, *J* = 7.5, NHCH_2C$\underline{H}_2$); 3.17–3.24 (4H, m, N(CH_2)$_2$ morpholine); 3.53 (2H, s, 1-CH_2); 3.70–3.76 (2H, m, NHC$\underline{H}_2$); 3.76–3.82 (4H, m, O(CH_2)$_2$ morpholine); 4.68 (2H, s, 4-CH_2); 7.11–7.20 (1H, m, H Ph); 7.21–7.28 (4H, m, H Ph); 7.47 (1H, br. t, *J* = 5.5, NH). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 26.6 (2CH_3); 34.9 (NHCH_2); 37.0 (1-CH_2); 41.9 (C$\underline{H}_2$Ph); 50.0 (3,5-CH_2 morpholine); 59.1 (4-CH_2); 66.0 (2,6-CH_2 morpholine); 69.1 (C-2); 107.8; 118.5; 120.0; 125.4 (C-4 Ph); 127.7 (C-3,5 Ph); 128.3 (C-2,6 Ph); 139.2 (C-1 Ph); 142.8; 154.6; 155.7; 158.5; 158.6 (C-8); 166.6 (C-10). Found, %: C 62.25; H 6.05; N 13.54; S 12.37. $C_{27}H_{31}N_5O_2S_2$. Calculated, %: C 62.16; H 5.99; N 13.42; S 12.29.

***N*-Hexyl-2,2-dimethyl-10-methylsulfanyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidin-8-amine (7d)**. Yield 1.20 g (80%), white crystals, mp 231–232°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91 (3H, t, *J* = 6.6, $CH_2C\underline{H}_3$); 1.28–1.45 (6H, m, $CH_3(C\underline{H}_2)_3$); 1.34 (6H, s, 2CH_3); 1.61–1.71 (2H, m, NHCH_2C$\underline{H}_2$); 2.52 (3H, s, SCH_3); 3.15–3.25 (4H, m, N(CH_2)$_2$ morpholine); 3.46–3.56 (4H, m, NHC$\underline{H}_2$, 1-CH_2); 3.74–3.84 (4H, m, O(CH_2)$_2$ morpholine); 4.68 (2H, s, 4-CH_2); 7.30 (1H, br. t, *J* = 5.4, NH). ^{13}C NMR spectrum, δ, ppm: 13.4 ($CH_2\underline{C}H_3$); 13.6 (SCH_3); 22.0 ($\underline{C}H_2CH_3$); 26.1 (CH_2); 28.7 (CH_2); 31.0 (CH_2); 26.6 (2CH_3); 37.0 (1-CH_2); 40.1 (NHCH_2); 50.0 (3,5-CH_2 morpholine); 59.1 (4-CH_2); 66.0 (2,6-CH_2 morpholine); 69.0 (C-2); 107.7; 118.5; 120.0; 142.8; 154.4; 155.8; 158.5 (C Ar, C-8); 166.5 (C-10). Found, %: C 59.93; H 6.98; N 13.81; S 12.67. $C_{25}H_{35}N_5O_2S_2$. Calculated, %: C 59.85; H 7.03; N 13.96; S 12.78.

10-Benzylsulfanyl-2,2-dimethyl-8-(4-methylpiperazin-1-yl)-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (7e). Yield 1.40 g (81%), white crystals, mp 206–207°C. ^{1}H NMR spectrum, δ, ppm: 1.21 (6H, s, 2CH_3); 2.30 (3H, s, NCH_3); 2.46–2.55 (4H, m, N(CH_2)$_2$ piperazine); 3.16–3.22 (4H, m, N(CH_2)$_2$ morpholine); 3.41 (2H, s, 1-CH_2); 3.75–3.80 (4H, m, O(CH_2)$_2$ morpholine); 3.89–3.96 (4H, m, N(CH_2)$_2$ piperazine); 4.44 (2H, s, SCH_2); 4.64 (2H, s,

4-CH_2); 7.15–7.29 (3H, m, H Ph); 7.37–7.43 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 26.4 (2CH_3); 34.3 (SCH_2); 37.1 (1-CH_2); 45.2 (NCH_3, 3,5-CH_2 piperazine); 49.8 (3,5-CH_2 morpholine); 54.1 (2,6-CH_2 piperazine); 59.0 (4-CH_2); 65.9 (2,6-CH_2 morpholine); 68.9 (C-2); 107.1; 118.7; 118.8; 126.2 (C-4 Ph); 127.7 (C-3,5 Ph); 127.8 (C-2,6 Ph); 137.8 (C-1 Ph); 143.1; 156.4 (C-10); 156.6; 156.9; 158.3; 159.1 (C-8). Found, %: C 62.36; H 6.25; N 14.69; S 11.03. $C_{30}H_{36}N_6O_2S_2$. Calculated, %: C 62.47; H 6.29; N 14.57; S 11.12.

***N*-Benzyl-10-benzylsulfanyl-2,2-dimethyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidin-8-amine (7f)**. Yield 1.45 g (83%), white crystals, mp 195–196°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.23 (6H, s, 2CH_3); 3.17–3.22 (4H, m, N(CH_2)$_2$ morpholine); 3.42 (2H, s, 1-CH_2); 3.75–3.81 (4H, m, O(CH_2)$_2$ morpholine); 4.40 (2H, s, SCH_2); 4.66 (2H, s, 4-CH_2); 4.76 (2H, d, *J* = 5.7, NHCH_2); 7.14–7.31 (6H, m, H Ph); 7.33–7.40 (4H, m, H Ph); 8.09 (1H, br. t, *J* = 5.7, NH). ^{13}C NMR spectrum, δ, ppm: 26.4 (2CH_3), 34.2 (SCH_2); 36.9 (1-CH_2); 43.5 ($NHCH_2$); 49.9 (3,5-CH_2 morpholine); 59.0 (4-CH_2); 65.9 (2,6-CH_2 morpholine); 68.9 (C-2); 118.5; 119.8; 126.0; 127.6 (4CH Ph); 127.8 (2CH Ph); 127.9 (4CH Ph); 138.2 (C Ph); 139.2 (C); 142.8; 154.7; 155.8; 156.8; 158.6 (C-8); 158.7(C-10). Found, %: C 65.77; H 5.76; N 11.91; S 10.86. $C_{32}H_{33}N_5O_2S_2$. Calculated, %: C 65.84; H 5.70; N 12.00; S 10.99.

***N*-Butyl-*N*-ethyl-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8-amine (7g)**. Yield 1.00 g (73%), light-yellow crystals, mp 119–120°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.3, CH_2CH_3); 1.30 (3H, t, *J* = 7.0, NCH_2CH_3); 1.38–1.51 (2H, m, CH_2CH_3); 1.66–1.78 (4H, m, 2,3-CH_2); 1.84–1.91 (2H, m, 4-CH_2); 1.91–1.99 (4H, m, 3,4-CH_2 pyrrolidine); 2.51 (3H, s, SCH_3); 2.71 (2H, t, *J* = 5.9, 1-CH_2); 3.52–3.62 (6H, m, NCH_2CH_2, N(CH_2)$_2$ pyrrolidine); 3.64–3.71 (2H, m, NCH_2CH_2); 3.76 (2H, q, *J* = 7.0, NCH_2CH_3). ^{13}C NMR spectrum, δ, ppm: 13.4 (NCH_2CH_3); 13.5 (SCH_3); 19.5 (CH_2CH_3); 21.6 (2-CH_2); 22.3 (3-CH_2); 25.1 (3,4-CH_2 pyrrolidine); 27.2 (4-CH_2); 27.4 (1-CH_2); 30.7 (CH_2); 40.1 (CH_2); 43.2 (CH_2); 48.0 (CH_2); 49.7 (2,5-CH_2 pyrrolidine); 104.0; 116.5; 117.3; 145.3; 155.7; 157.4; 158.0; 159.8 (C-8); 165.1 (C-10). Found, %: C 63.37; H 7.26; N 15.24; S 14.17. $C_{24}H_{33}N_5S_2$. Calculated, %: C 63.26; H 7.30; N 15.37; S 14.07.

***N*-(2-Furylmethyl)-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinolin-8-amine (7h)**. Yield 1.00 g (74%), light-yellow crystals, mp 159–160°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.70–1.79 (2H, m, 2-CH_2); 1.84–1.92 (2H, m, 3-CH_2); 1.92–1.99 (4H, m, 3,4-CH_2 pyrrolidine); 2.53 (3H, s, SCH_3); 2.71 (2H, t, *J* = 5.7, 4-CH_2); 3.49–3.65 (6H, m, N(CH_2)$_2$ pyrrolidine, 1-CH_2); 4.70 (2H, d, *J* = 5.6, NHCH_2); 6.25–6.32 (2H, m, H-3,4 Fur); 7.39 (1H, dd, *J* = 1.7, *J* = 0.7, H-5 Fur); 7.66 (1H, br. t, *J* = 5.6, NH). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 21.5 (2-CH_2); 22.4 (3-CH_2); 25.1 (3,4-CH_2 pyrrolidine); 27.1 (4-CH_2); 27.2 (1-CH_2); 36.7 ($NHCH_2$); 49.8 (2,5-CH_2 pyrrolidine); 106.2; 106.6 (CH Fur); 109.8 (CH Fur); 117.2 (2C); 140.7 (CH Fur); 145.2; 152.5; 155.4; 155.8; 158.4; 159.6 (C-8); 165.7 (C-10). Found, %: C 61.25; H 5.64; N 15.42; S 14.34. $C_{23}H_{25}N_5OS_2$. Calculated, %: C 61.17; H 5.58; N 15.51; S 14.20.

10-Benzylsulfanyl-5-(morpholin-4-yl)-8-(pyrrolidin-1-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinoline (7i). Yield 1.29 g (83%), white crystals, mp 198–200°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.69–1.79 (2H, m, 2-CH_2); 1.81–1.91 (2H, m, 3-CH_2); 2.01–2.10 (4H, m, 3,4-CH_2 pyrrolidine); 2.70 (2H, t, *J* = 5.2, 4-CH_2); 3.17–3.24 (4H, m, N(CH_2)$_2$ morpholine); 3.53 (2H, t, *J* = 6.5, 1-CH_2); 3.74–3.80 (4H, m, O(CH_2)$_2$ morpholine); 3.83–3.91 (4H, m, N(CH_2)$_2$ pyrrolidine); 4.41 (2H, s, SCH_2); 7.14–7.28 (3H, m, HPh); 7.37–7.42 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 21.8 (2-CH_2); 22.3 (3-CH_2); 24.6 (4-CH_2); 25.1 (3,4-CH_2 pyrrolidine); 26.8 (1-CH_2); 34.5 (SCH_2); 47.5 (2,5-CH_2 pyrrolidine); 49.8 (3,5-CH_2 morpholine); 66.0 (2,6-CH_2 morpholine); 108.9; 117.8; 118.6; 126.7 (C-4 Ph); 127.5 (C-3,5 Ph); 127.9 (C-2,6 Ph); 137.8 (C-1 Ph); 143.6; 157.4; 158.3; 158.7; 159.2 (C-8); 166.1 (C-10). Found, %: C 65.08; H 5.99; N 13.67; S 12.28. $C_{28}H_{31}N_5OS_2$. Calculated, %: C 64.96; H 6.04; N 13.53; S 12.39.

9-Methylsulfanyl-4-(morpholin-4-yl)-7-(pyrrolidin-1-yl)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]-pyrimidine (7j). Yield 1.03 g (80%), cream-colored crystals, mp 241–242°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.00–2.10 (4H, m, 3,4-CH_2 pyrrolidine); 2.12–2.24 (2H, m, 2-CH_2); 2.52 (3H, s, SCH_3); 2.95 (2H, t, *J* = 7.2, 3-CH_2); 3.47 (2H, t, *J* = 7.5, 1-CH_2); 3.47–3.52 (4H, m, N(CH_2)$_2$ morpholine); 3.73–3.78 (4H, m, O(CH_2)$_2$ morpholine); 3.82–3.89 (4H, m, N(CH_2)$_2$ pyrrolidine). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 25.1 (2-CH_2); 25.2 (3,4-CH_2 pyrrolidine), 31.4 (3-CH_2); 31.7 (1-CH_2); 49.4 (2,5-CH_2 pyrrolidine); 49.8 (3,5-CH_2 morpholine); 65.9 (2,6-CH_2 morpholine); 106.8; 117.5; 123.6; 152.1; 156.4; 156.9; 157.3; 158.4 (C-7); 165.8 (C-9). Found, %: C 59.08; H 5.83; N 16.49; S 14.88. $C_{21}H_{25}N_5OS_2$. Calculated, %: C 58.99; H 5.89; N 16.38; S 15.00.

9-Methylsulfanyl-4,7-bis(morpholin-4-yl)-2,3-dihydro-1*H*-cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (7k). Yield 1.11 g (83%), light-pink crystals, mp 240–241°C. ^{1}H NMR spectrum, δ, ppm: 2.14–2.25 (2H, m, 2-CH_2); 2.55 (3H, s, SCH_3); 2.98 (2H, t, *J* = 7.2, 3-CH_2); 3.48 (2H, t, *J* = 7.4, 1-CH_2); 3.49–3.55 (4H, m, 4-N(CH_2)$_2$ morpholine); 3.73–3.81 (8H, m, 7-N(CH_2)$_2$ morpholine, 4-morpholine). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 25.1 (2-CH_2); 31.5 (3-CH_2); 31.9 (1-CH_2); 45.5 (3,5-CH_2 4-(morpholin-4-yl)); 47.4 (3,5-CH_2 7-(morpholin-4-yl)); 65.8 (2,6-CH_2 4-(morpholin-4-yl)); 65.9 (2,6-CH_2 7-(morpholin-4-yl)); 106.3; 117.0; 123.8; 152.6; 156.6; 156.7; 157.9; 158.6 (C-7); 166.1 (C-9). Found, %: C 56.98; H 5.72; N 15.88; S 14.32. $C_{21}H_{25}N_5O_2S_2$. Calculated, %: C 56.86; H 5.68; N 15.79; S 14.46.

Preparation of compounds 8a–f (General method). Compound **6a–e** (2 mmol) was added to sodium ethoxide solution obtained from sodium metal (46 mg, 2 mmol) and anhydrous ethanol (15 ml). The mixture was refluxed for 10 h. The crystals that formed after cooling were filtered off and washed with water, then recrystallized from a 1:2 mixture of $CHCl_3$ and EtOH.

8-Ethoxy-2,2-dimethyl-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidine (8a). Yield 0.66 g (77%), light-yellow crystals, mp 188–189°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, s, $2CH_3$); 1.49 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.95–2.00 (4H, m, 3,4-CH_2 pyrrolidine); 2.58 (3H, s, SCH_3); 3.43 (2H, s, 1-CH_2); 3.62–3.67 (4H, m, $N(CH_2)_2$ pyrrolidine); 4.61 (2H, q, *J*=.1, $OC\underline{H}_2CH_3$); 4.80 (2H, s, 4-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 14.1 ($CH_2\underline{C}H_3$); 25.0 (3,4-CH_2 pyrrolidine); 26.5 ($2CH_3$); 37.1 (1-CH_2); 49.8 (2,5-CH_2 pyrrolidine); 59.2 (4-CH_2); 62.7 ($\underline{C}H_2CH_3$); 68.8 (C-2); 108.7; 115.9; 116.1; 142.8; 156.6; 156.8; 158.5; 161.2 (C-8), 166.3 (C-10). Found, %: C 58.49; H 6.15; N.15; S 14.78. $C_{21}H_{26}N_4O_2S_2$. Calculated, %: C 58.58; H 6.09; N 13.01; S 14.89.

8-Methoxy-2,2-dimethyl-10-methylsulfanyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidine (8b). Yield 0.68 g (79%), white crystals, mp 209–210°C. ^{1}H NMR spectrum, δ, ppm: 1.35 (6H, s, $2CH_3$); 2.61 (3H, s, SCH_3); 3.22–3.28 (4H, m, $N(CH_2)_2$ morpholine); 3.49 (2H, s, 1-CH_2); 3.76–3.81 (4H, m, $O(CH_2)_2$ morpholine); 4.16 (3H, s, OCH_3); 4.70 (2H, s, 4-CH_2). ^{13}C NMR spectrum, δ, ppm: 13.7 (SCH_3); 26.1 ($2CH_3$); 37.0 (1-CH_2); 49.7 (3,5-CH_2 morpholine); 54.2 (OCH_3); 59.4 (4-CH_2); 66.1 (2,6-CH_2 morpholine); 68.9 (C-2); 108.6; 119.5; 120.3; 143.7; 155.6; 156.4; 157.5; 158.8 (C-8); 166.1 (C-10). Found, %: C 55.60; H 5.64; N 12.83; S 14.97. $C_{20}H_{24}N_4O_3S_2$. Calculated, %: C 55.53; H 5.59; N 12.95; S 14.83.

8-Isopropoxy-2,2-dimethyl-10-methylsulfanyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidine (8c). Yield 0.71 g (77%), white crystals, mp 219–220°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, s, $2CH_3$); 1.49 (6H, d, *J* = 6.2, $CH(C\underline{H}_3)_2$); 2.59 (3H, s, SCH_3); 3.22–3.28 (4H, m, $N(CH_2)_2$ morpho-line); 3.49 (2H, s, 1-CH_2); 3.76–3.82 (4H, m, $O(CH_2)_2$ morpholine); 4.68 (2H, s, 4-CH_2); 5.61 (1H, sept, *J* = 6.2, OCH). ^{13}C NMR spectrum, δ, ppm: 13.5 (SCH_3); 25.1 ($CH(\underline{C}H_3)_2$); 26.7 ($2CH_3$); 37.1 (1-CH_2); 49.8 (3,5-CH_2 morpholine); 59.3 (4-CH_2); 66.0 (2,6-CH_2 morpholine); 65.7 (OCH); 69.0 (C-2); 108.4; 118.7; 121.4; 141.6; 153.8; 156.6; 158.2; 158.7 (C-8); 166.4 (C-10). Found, %: C 57.45; H 6.19; N 12.27; S 13.84. $C_{22}H_{28}N_4O_3S_2$. Calculated, %: C 57.37; H 6.13; N 12.16; S 13.92.

10-Benzylsulfanyl-8-ethoxy-2,2-dimethyl-5-(morpholin-4-yl)-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidine (8d). Yield 0.84 g (80%), white crystals, mp 178–179°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (6H, s, $2CH_3$); 1.50 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$); 3.21–3.26 (4H, m, $N(CH_2)_2$ morpholine); 3.38 (2H, s, 1-CH_2); 3.75–3.80 (4H, m, $O(CH_2)_2$ morpholine); 4.48 (2H, s, SCH_2); 4.63 (2H, q, *J* = 7.0, $OC\underline{H}_2CH_3$); 4.65 (2H, s, 4-CH_2). 7.17–7.30 (3H, m, H Ph); 7.39–7.45 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 14.0 ($CH_2\underline{C}H_3$); 26.4 ($2CH_3$); 34.5 (SCH_2); 37.0 (1-CH_2); 49.8 (3,5-CH_2 morpholine); 59.1 (4-CH_2); 62.5 ($\underline{C}H_2CH_3$); 65.9 (2,6-CH_2 morpholine); 68.9 (C-2); 109.9; 118.6; 118.8; 126.3 (C-4 Ph); 127.8 (C-3,5 Ph); 127.9 (C-2,6 Ph); 137.3 (C-1 Ph); 142.9; 157.3; 159.1; 159.8; 162.4 (C-8); 166.1 (C-10). Found, %: C 62.13; H 5.72; N 10.63; S 12.35. $C_{27}H_{30}N_4O_3S_2$. Calculated, %: C 62.04; H 5.79; N 10.72; S 12.27.

8-Ethoxy-10-methylsulfanyl-5-(pyrrolidin-1-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinoline (8e). Yield 0.71 g (88%), yellow crystals, mp 206–207°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$); 1.71–1.80 (2H, m, 2-CH_2); 1.86–1.93 (2H, m, 3-CH_2); 1.93–2.00 (4H, m, 3,4-CH_2 pyrrolidine); 2.59 (3H, s, SCH_3); 2.74 (2H, t, *J* = 5.9, 4-CH_2); 3.54 (2H, t, *J* = 6.3, 1-CH_2); 3.60–3.66 (4H, m, $N(CH_2)_2$ pyrrolidine); 4.60 (2H, q, *J* = 7.0, $OC\underline{H}_2CH_3$). ^{13}C NMR spectrum, δ, ppm: 13.6 (SCH_3); 14.0 ($CH_2\underline{C}H_3$); 21.3 (2-CH_2); 22.4 (3-CH_2); 25.0 (3,4-CH_2 pyrrolidine); 26.8 (4-CH_2); 27.1 (1-CH_2); 49.7 (2,5-CH_2 pyrrolidine); 62.4 ($\underline{C}H_2CH_3$); 113.7; 115.8; 119.4; 143.6; 152.8; 157.5; 159.4; 160.5 (C-8), 166.1 (C-10). Found, %: C 59.90; H 6.10; N 14.08; S 16.14. $C_{20}H_{24}N_4OS_2$. Calculated, %: C 59.97; H 6.04; N 13.99; S 16.01.

10-Benzylsulfanyl-8-ethoxy-5-(morpholin-4-yl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquinoline (8f). Yield 0.78 g (79%), white crystals, mp 236–237°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.50 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.71–1.81 (2H, m, 2-CH_2); 1.84–1.95 (2H, m, 3-CH_2); 2.66–2.74 (2H, m, 4-CH_2); 3.22–3.30 (4H, m, $N(CH_2)_2$ morpholine); 3.45–3.54 (2H, m, 1-CH_2); 3.74–3.83 (4H, m, $O(CH_2)_2$ morpholine); 4.47 (2H, s, SCH_2); 4.62 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 7.17–7.32 (3H, m, H Ph); 7.38–7.46 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 14.0 ($CH_2\underline{C}H_3$); 22.1 (2-CH_2); 22.4 (3-CH_2); 26.8 (4-CH_2); 27.1 (1-CH_2); 34.4 (SCH_2); 49.7 (3,5-CH_2 morpholine); 62.4 ($\underline{C}H_2CH_3$); 65.8 (2,6-CH_2 morpholine); 108.7; 118.5; 118.8; 126.4 (C-4 Ph); 127.7 (C-3,5 Ph); 127.8 (C-2,6 Ph); 137.4 (C-1 Ph); 142.7; 157.1; 159.4; 160.2; 162.8 (C-8); 166.5 (C-10). Found, %: C 63.46; H 5.78; N 11.46; S 13.14. $C_{26}H_{28}N_4O_2S_2$. Calculated, %: C 63.39; H 5.73; N 11.37; S 13.02.

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