Transformations of tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones in the presence of alkynes bearing electron-withdrawing substituents

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Tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidines in the presence of activated alkynes were transformed into mixtures of pyrimido[5′,4′:4,5]thieno[3,2-*d*]azocines and spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidines].

Key words: pyridothienopyrimidine, ring opening, expansion of the tetrahydropyridine ring, pyrimidothieno[3,2-*d*]azocine, spiro[pyridinethieno[2,3-*d*]pyrimidine].

Tandem expansion of the tetrahydropyridine ring in fused tetrahydropyridines under the action of activated alkynes (containing electron-withdrawing groups) can serve as a general synthetic approach to fused azocines. This reaction underlies efficient preparative methods for the synthesis of tetrahydropyrrolo[2,3-*d*]azocines,[1] tetrahydrothieno[3,2-*d*]azocines,[2] tetrahydroazocino[4,5-*b*]- and [5,4-*b*]indoles,[3] tetrahydropyrimido[4,5-*d*]azocines,[4] and tetrahydrobenzoazocines.[5]

The pathway of transformations of tetrahydropyridines containing an aryl(hetaryl)methylamino fragment largely depends on the electronic effects of the annulated aromatic ring as well as on the solvent nature. Reactions of 2-trifluoroacetamidotetrahydrothieno[2,3-*c*]pyridines with alkynes in methanol and acetonitrile give tetrahydrothieno[3,2-*d*]azocines through expansion of the tetrahydropyridine ring.[2] Annulation of the benzene ring to the thiophene ring of tetrahydrothieno[2,3-*c*]pyridines makes such systems less reactive in reactions with alkynes. Benzothieno[2,3-*c*]pyridines react only with dimethyl acetylenedicarboxylate (DMAD) in acetonitrile to give spiro[benzothiophene-3,4′-pyridines] in moderate yields.[6] 1-Aryltetrahydrobenzothieno[2,3-*c*]pyridines react with both DMAD and terminal alkynes (methyl propiolate and acetylacetylene). These reactions produce mixtures of benzothieno[3,2-*d*]azocines, spiro[benzothiophene-3,4′-pyridines], and various 1-vinyl derivatives as a result of the Stevens rearrangement.[7] In methanol, the tetrahydropyridine ring undergoes opening under the action of solvent molecules and the reaction products also include 2-methoxybenzylbenzothiophenes. In connection with this, it was interesting to find out how annulation of the pyrimidin-4-one fragment to the thiophene ring of tetrahydrothieno[2,3-*c*]pyridine would influence the pathway of tandem transformations and the reactivity of the resulting tricyclic heterocycles.

Starting from the Gewald tetrahydrothienopyridines[8] **1**—**4**, triethyl orthoformate, and an arylamine, we obtained tetrahydropyridothienopyrimidines **5**—**11** (Scheme 1). Pyridothienopyrimidines **5**—**7** and **9** were prepared in one step. In the synthesis of compounds **8**, **10**, and **11**, the major reaction products were amidines **12**—**14**, which were isolated from the reaction mixtures and transformed into target pyridothienopyrimidines **8**, **10**, and **11** under the action of sodium amide in anhydrous toluene.

We studied reactions of tetrahydropyridothienopyrimidines **5**—**11** with DMAD, methyl propiolate (MP), and acetylacetylene (AA) in acetonitrile and methanol (Scheme 2, Table 1).

It turned out that pyridothienopyrimidines **5**—**11** are substantially less reactive than, and their tandem transformations in reactions with alkynes follow different pathways compared to, the corresponding substituted tetrahydrothienopyridines.[2] Compounds **5**—**11** react with a 3—7-fold excess of an alkyne in boiling methanol or acetonitrile to give mixtures of spiro[pyridinethieno-[2,3-*d*]pyrimidines] **15a**—**l** (major products) and pyrimidothieno[3,2-*d*]azocines **16a**—**l** formed by opening and expansion of the tetrahydropyridine ring, respectively. Both the yields of the target products and the reactivity of compounds **5**—**11** depend on the substituents in their phenyl ring. Compounds **5** and **6** (Ar = Ph) slowly react with

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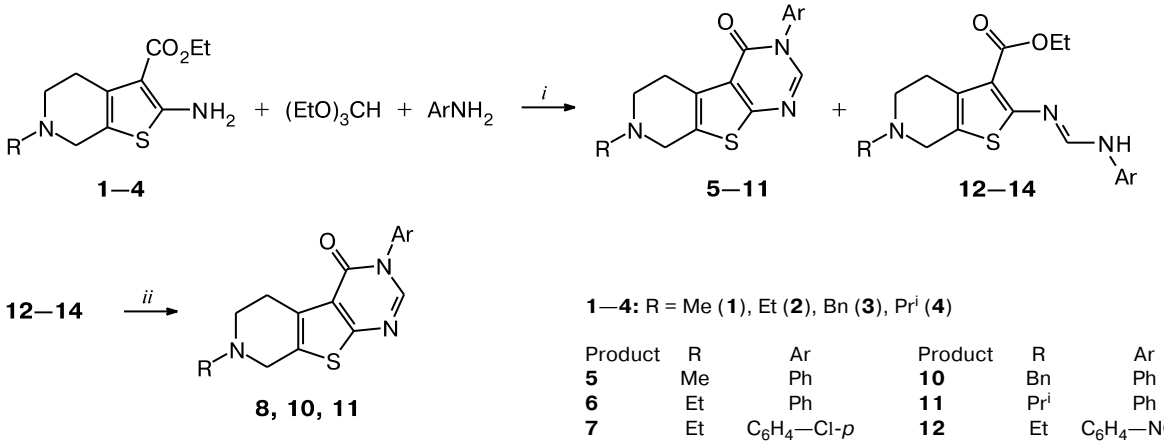
Scheme 1

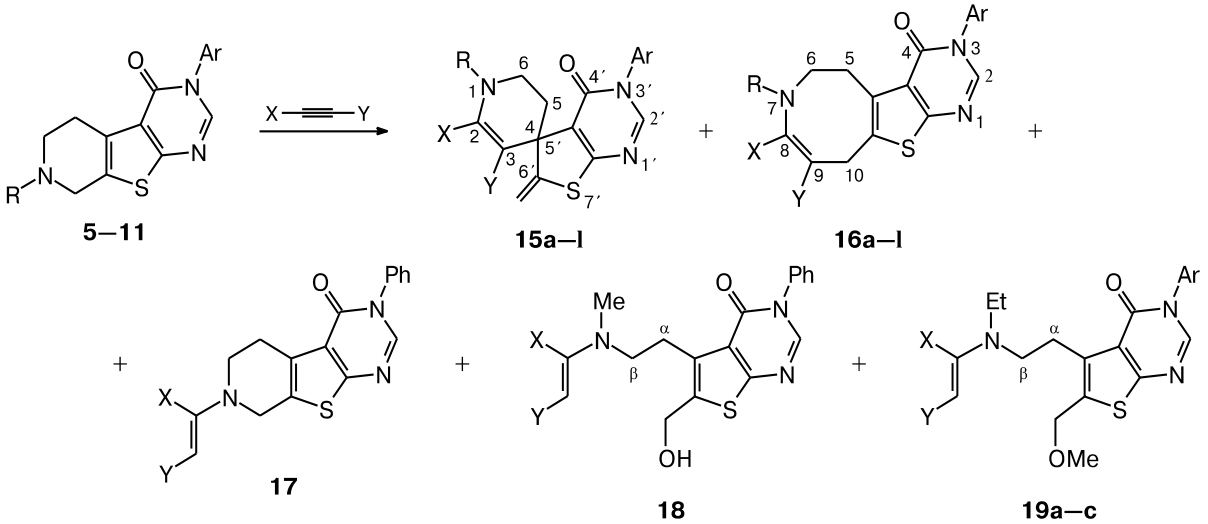


Conditions: *i*. toluene, reflux; *ii*. $NaNH_2$, toluene.

1—4: R = Me (**1**), Et (**2**), Bn (**3**), Pr^i (**4**)

Product	R	Ar	Product	R	Ar
5	Me	Ph	**10**	Bn	Ph
6	Et	Ph	**11**	Pr^i	Ph
7	Et	C_6H_4—Cl-*p*	**12**	Et	C_6H_4—NO_2-*p*
8	Et	C_6H_4—NO_2-*p*	**13**	Bn	Ph
9	Et	C_6H_4—OMe-*o*	**14**	Pr^i	Ph

Scheme 2



Product	R	Ar	X	Y	Product	R	Ar	X	Y
15, **16**									
a	Me	Ph	CO_2Me	CO_2Me	**g**	Et	C_6H_4—NO_2-*p*	H	CO_2Me
b	Et	Ph	CO_2Me	CO_2Me	**h**	Et	C_6H_4—NO_2-*p*	H	COMe
c	Et	C_6H_4—Cl-*p*	CO_2Me	CO_2Me	**i**	Et	C_6H_4—OMe-*o*	CO_2Me	CO_2Me
d	Et	C_6H_4—Cl-*p*	H	CO_2Me	**j**	Et	C_6H_4—OMe-*o*	H	CO_2Me
e	Et	C_6H_4—Cl-*p*	H	COMe	**k**	Et	C_6H_4—OMe-*o*	H	COMe
f	Et	C_6H_4—NO_2-*p*	CO_2Me	CO_2Me	**l**	Pr^i	Ph	CO_2Me	CO_2Me

17, 18: X = Y = CO_2Me
19: X = Y = CO_2Me, Ar = C_6H_4—Cl-*p* (**a**), C_6H_4—OMe-*o* (**b**); X = H, Y = CO_2Me, Ar = C_6H_4—OMe-*o* (**c**)

DMAD in acetonitrile at 20 °C. The reaction in boiling acetonitrile gives a mixture we fail to separate by column chromatography.

Reactions of compound **5** with DMAD in CH_2Cl_2 give spiro compound **15a**, 7-vinylpyridothienopyrimidine **17** (11%), and 6-hydroxymethylthienopyrimidine **18** (1%). The formation of the last product is probably due to the opening of the tetrahydropyridine ring under the action of water contained in CH_2Cl_2. 7-Vinylpyridothienopyrimidine **17** was also obtained in a reaction of compound **10** with DMAD in both room-temperature and boiling acetonitrile; the yields were 14 and 6%, respectively.

Table 1. Yields of spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidines] **15a—l** and pyrimido[5′,4′:4,5]thieno[3,2-*d*]azocines **16a—l** in tandem transformations of pyridothienopyrimidines **5—11** with activated alkynes

Compound	Alkyne	Solvent (T/°C)	τ*	Yield (%)	
				Azocine	Spiran
5	DMAD	MeCN (20)	6 days	**16a** (traces)	**15a** (25)
		CH_2Cl_2 (20)	10 days	—	**15a** (11)
6	DMAD	MeCN (20)	7 days	**16b** (6)	**15b** (18)
7	DMAD	MeCN	65 h	**16c** (14)	**15c** (44)
		MeOH	30 h	**16c** (6)	**15c** (24)
	MP	MeCN	21 h	**16d** (traces)	**15d** (57)
		MeOH	8 h	**16d** (11)	**15d** (62)
	AA	MeCN	20 h	**16e** (7)	**15e** (37)
8	DMAD	MeCN	2 h	**16f** (12)	**15f** (28)
		MeOH	34 h	**16f** (14)	**15f** (17)
	MP	MeCN (20)	2 days	**16g** (9)	**15g** (25)
		MeOH	3 h	**16g** (3)	**15g** (51)
	AA	MeCN (20)	5 days	**16h** (traces)	**15h** (9)
9	DMAD	MeCN (20)	13 days	**16i** (18)	**15i** (45)
		MeOH	71 h	**16i** (traces)	**15i** (50)
	MP	MeCN	20 h	**16j** (12)	**15j** (30)
		MeOH	122 h	**16j** (traces)	**15j** (8)
	AA	MeCN	11 h	**16k** (10)	**15k** (46)
11	DMAD	MeCN (20)	12 days	**16l** (11)	**15l** (57)

* τ is the reaction time.

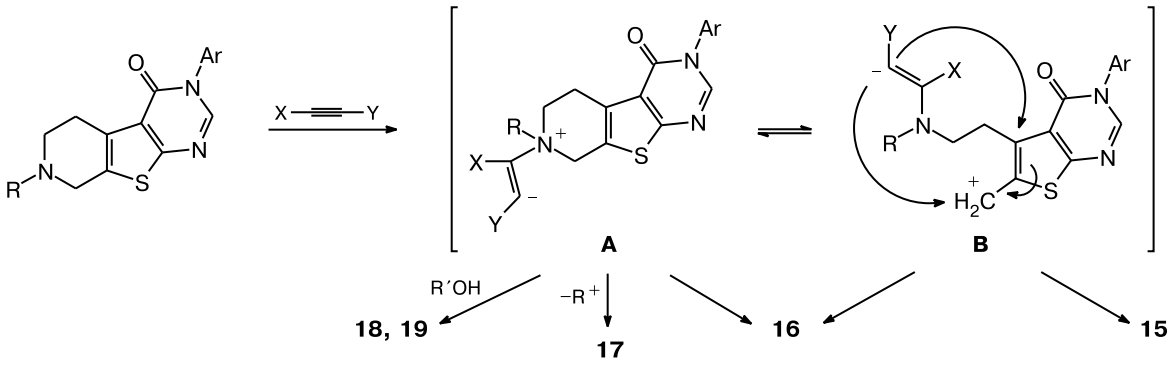
Compounds **7—9** containing a substituted phenyl group react with alkynes in both methanol and acetonitrile more readily and selectively than do compounds **5** and **6** (with the exception that pyridothienopyrimidines **7** and **9** do not react with acetylacetylene in methanol). Note that the reactions of compounds **7** and **9** with DMAD and that of compound **9** with methyl propiolate in boiling methanol give the corresponding azocines and spiro compounds as well as 6-methoxymethylthienopyrimidines **19a—c** by opening of the tetrahydropyridine ring under the action of methanol (the yields are 7, 12, and 44%, respectively).

Compounds **5—11** in reactions with alkynes undergo the following tandem transformations. The first step is the formation of ammonium zwitterion **A** (Scheme 3), which transforms itself into zwitterion **B** through the cleavage of the C(1)—N bond. An intramolecular nucleophilic attack of the anionic center in zwitterion **B** results in closure of spiro compound **15**. Azocines **16** can be produced from both **A** and **B** by a nucleophilic attack on the C(1) atom. The formation of 7-vinylpyridothienopyrimidine **17** from **A** results from dealkylation of the ammonium center. Hydroxymethyl and methoxymethyl derivatives **18** and **19** are usual products of the decomposition of zwitterion **A** in alcohols and solvents containing some water.

The structures of spiro compounds **15a—l** and azocines **16a—l** were confirmed by spectroscopic data. Their mass spectra show molecular ion peaks corresponding to their molecular formulas. The IR spectra contain absorption bands at 1747—1621 cm^{-1} (C=O stretches of the amide, ester, and oxo groups). The ^1H NMR spectra of spiro compounds **15a—l** show two doublets at δ 5.02—5.33 from the methylene protons with ^2J = 1.3—2.0 Hz. The ^1H NMR spectra of azocines **16d**,**e**,**g**,**h**,**j**,**k** exhibit a singlet at δ 7.32—7.48 from the proton of the enamine fragment.

The structure of spiro compound **15a** was examined by X-ray diffraction (Fig. 1). Structure **15a** contains three (dihydropyrimidine, dihydrothiophene, and tetrahydropyridine) rings. The dihydropyrimidine ring is virtually planar, while the dihydrothiophene and tetrahydropyridine ones are in the conformations of slightly distorted *envelope* (the C(2) atom deviates from the mean-square plane of the other ring atoms by 0.397(2) Å) and *sofa* (the C(5′) atom deviates from the mean-square plane of the

Scheme 3



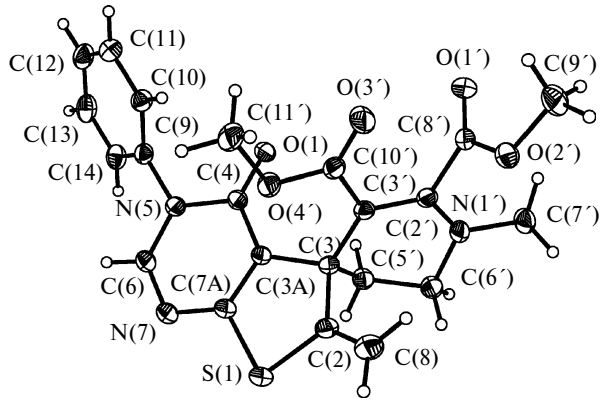


Fig. 1. Molecular structure of spiro compound **15a** with atomic displacement ellipsoids (p = 40%).

other ring atoms by 0.651(2) Å), respectively. Because of steric hindrances, the methoxycarbonyl substituent at the C(3′) atom is coplanar with the plane of the tetrahydropyridine ring, while the methoxycarbonyl substituent at the C(2′) atom is nearly perpendicular to this plane (the angle between the corresponding planes is 84.95(6)°).

The phenyl substituent makes an angle of 50.65(5)° with the plane of the dihydropyrimidine ring, which is probably due to the intermolecular attractive interactions n(S(1))...π(C(9)—C(10)) [1 − x, 1 − y, 2 − z] (the S(1)...C(9A) and S(1)...C(10A) distances are 3.433(2) and 3.503(2) Å, respectively). These interactions give rise to centrosymmetric dimers in the crystal (Fig. 2). The dimers are additionally stabilized by the intermolecular interactions π(C(6)=N7)...π(C(6)=N(7)) [1 − x, 1 − y, 2 − z] (the C(6)...N(7A) and N(7)...C(6A) distances are 3.126(2) Å) (Fig. 2).

In the crystal, dimers are united into a 3D framework through weak intermolecular hydrogen bonds C—H...O. Spiro compound **15a** contains the asymmetric C(3) atom. The crystal of **15a** is a racemate.

To sum up, we demonstrated that annulation of the pyrimidine ring to thienopyridine provides a variety of transformations of tetrahydropyridothienopyrimidines in reactions with alkynes.

Experimental

The IR spectra of the compounds obtained were recorded on an Infralum FT-801 FTIR spectrometer in KBr pellets or thin films (for liquid samples). Mass spectra were measured on a Finnigan MAT 95 XL GC-MS instrument (direct inlet probe, EI, 70 eV). LC-MS spectra were recorded on a system composed of an Agilent 1100 Series liquid chromatograph, an Agilent Technologies LC/MSD VL mass spectrometer (ESI, APCI, ELSD Sedex 75). High-resolution mass spectra were measured on a JEOL JMS-T100LP-DART 100 instrument (ESI, DART). ^{1}H and ^{13}C NMR spectra were recorded on Bruker (400 (^{1}H) and 100 MHz (^{13}C)) and JEOL JNM-ECA 600 instruments (600 (^{1}H) and 150 MHz (^{13}C)) in $CDCl_3$ with Me_4Si as the internal standard. For TLC, Sorbfil and Silufol plates were used (spots were visualized under UV light); for column chromatography, neutral alumina (Fluka, activity grade II, 60 mesh) and Acros 60E silica gel (0.04—0.06 mm).

X-ray diffraction study of compound 15a. Colorless prismatic crystals ($C_{22}H_{21}N_3O_5S$, M = 439.48, 0.15ч0.16ч0.22 mm) are monoclinic, space group $P2_1/n$; at 120(2) K: a = 9.7524(5) Å, b = 9.9873(6) Å, c = 21.4410(12) Å, β = 100.494(1)°, V = = 2053.4(2) Å^3, Z = 4, F(000) = 920, d_{calc} = 1.422 g cm^{-3}, μ = 0.199 mm^{-1}. The unit cell parameters and the intensities of 22 836 reflections (5922 independent reflections, R_{int} = 0.028) were measured on a Bruker SMART 1K CCD automatic diffractometer (λMo-$K\alpha$ radiation, graphite monochromator, φ and ω scan modes, θ_{max} = 30°). The structure was solved by direct methods and refined by the full-matrix least-squares method in the anisotropic approximation for non-hydrogen atoms. The hydrogen atoms were located geometrically and refined isotropically with fixed coordinates (riding model) and thermal pa-

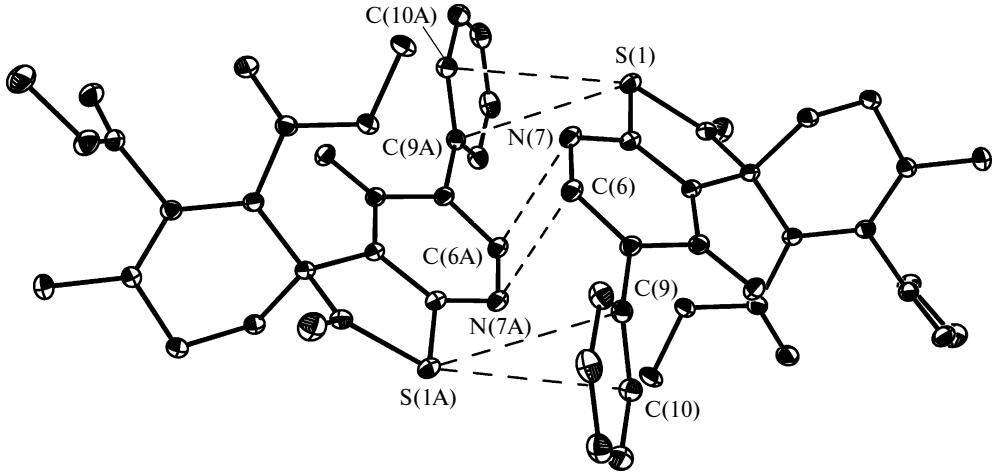


Fig. 2. Centrosymmetric dimers in structure **15a** (the hydrogen atoms are omitted). Attractive intermolecular interactions are indicated with dashed lines.

rameters (U_{iso}(H) = 1.5U_{equiv}(C) for Me groups; U_{iso}(H) = = 1.2U_{equiv}(C) for the other groups). Final residuals are $R_1 = 0.045$ for 4792 independent reflections with $I > 2\sigma(I)$ and $wR_2 = 0.121$ for all independent reflections; the number of parameters refined is 283, GOOF = 1.003. All calculations were performed with the SHELXTL program package.[9] The tables of the atomic coordinates, bond lengths, bond angles, and anisotropic thermal parameters for compound **15a** have been deposited with the Cambridge Crystallographic Data Center.

Synthesis of tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidines 5—7 and 9 (general procedure). A solution of thieno[2,3-*c*]-pyridine **1** or **2** (10 mmol) and triethyl orthoformate (12 mmol) in toluene (50 mL) was refluxed for 1.5—2 h. Then an appropriate aniline (50 mmol) was added and the reaction mixture was refluxed for 4—30 h. The course of the reactions was monitored by TLC. After the reaction was completed, the solvent was removed *in vacuo* and the residue was treated with ethyl acetate—diethyl ether. The resulting crystals of tetrahydropyrido[4′,3′:4,5]-thieno[2,3-*d*]pyrimidines **5**—**7** and **9** were filtered off and recrystallized from ethyl acetate—hexane.

7-Methyl-3-phenyl-5,6,7,8-tetrahydropyrido[4′,3′:4,5]-thieno[2,3-*d*]pyrimidin-4(3*H*)-one (5). Yield 67%, light yellow crystals, m.p. 178—179 °C, R_f 0.53 (Silufol, ethyl acetate). Found (%): C, 64.78; H, 5.15; N, 14.02. $C_{16}H_{15}N_3OS$. Calculated (%): C, 64.62; H, 5.08; N, 14.13. IR, ν/cm^{-1}: 1692 (C=O). ^{1}H NMR, δ: 2.51 (s, 3 H, N—Me); 2.77 (t, 2 H, C(6)H$_2$, J = 6.0 Hz); 3.15 (tt, 2 H, C(5)H$_2$, J = 6.0 Hz, J = 1.7 Hz); 3.66 (t, 2 H, C(8)H$_2$, J = 1.7 Hz); 7.39 (d, 2 H, Ph, J = 7.2 Hz); 7.48 (t, 1 H, Ph, J = 7.2 Hz); 7.53 (t, 2 H, Ph, J = 7.2 Hz); 7.99 (s, 1 H, C(2)H). MS, m/z (I_{rel} (%)): 297 [M]$^+$ (38), 296 (18), 254 (51), 253 (15), 104 (23), 78 (10), 77 (92), 51 (21), 43 (37), 42 (100).

7-Ethyl-3-phenyl-5,6,7,8-tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6). Yield 52%, light yellow crystals, m.p. 127—129 °C, R_f 0.50 (Silufol, ethyl acetate). Found (%): C, 65.63; H, 5.40; N, 13.52. $C_{17}H_{17}N_3OS$. Calculated (%): C, 65.57; H, 5.50; N, 13.49. IR, ν/cm^{-1}: 1698 (C=O). ^{1}H NMR, δ: 1.19 (t, 3 H, N—CH$_2$C<u>H</u>$_3$, J = 7.2 Hz); 2.65 (q, 2 H, N—C<u>H</u>$_2$Me, J = 7.2 Hz); 2.82 (t, 2 H, C(6)H$_2$, J = 5.7 Hz); 3.14 (tt, 2 H, C(5)H$_2$, J = 5.7 Hz, J = 1.7 Hz); 3.72 (t, 2 H, C(8)H$_2$, J = 1.7 Hz); 7.39 (d, 2 H, Ph, J = 7.0 Hz); 7.47—7.55 (m, 3 H, Ph); 7.98 (s, 1 H, C(2)H). MS, m/z (I_{rel} (%)): 311 [M]$^+$ (100), 310 (35), 296 (14), 255 (20), 254 (88), 253 (18), 104 (23), 77 (95), 56 (21), 42 (61).

3-(4-Chlorophenyl)-7-ethyl-5,6,7,8-tetrahydropyrido-[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7). Yield 53%, light yellow crystals, m.p. 180—181 °C, R_f 0.49 (Silufol, ethyl acetate). Found (%): C, 59.12; H, 4.60; N, 12.23. $C_{17}H_{16}ClN_3OS$. Calculated (%): C, 59.04; H, 4.66; N, 12.15. IR, ν/cm^{-1}: 1691 (C=O). ^{1}H NMR, δ: 1.20 (t, 3 H, N—CH$_2$C<u>H</u>$_3$, J = 7.1 Hz); 2.66 (q, 2 H, N—C<u>H</u>$_2$Me, J = 7.1 Hz); 2.82 (t, 2 H, C(6)H$_2$, J = 5.8 Hz); 3.13 (tt, 2 H, C(5)H$_2$, J = 5.8 Hz, J = 1.8 Hz); 3.72 (t, 2 H, C(8)H$_2$, J = 1.8 Hz); 7.35 (d, 2 H, Ph, J = 8.8 Hz); 7.51 (d, 2 H, Ph, J = 8.8 Hz); 7.95 (s, 1 H, C(2)H). MS, m/z (I_{rel} (%)): 345 [M]$^+$ (93), 344 (45), 330 (13), 290 (48), 288 (75), 253 (10), 140 (25), 138 (85), 113 (27), 111 (100), 76 (10), 75 (16), 56 (22), 42 (87).

7-Ethyl-3-(2-methoxyphenyl)-5,6,7,8-tetrahydropyrido-[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (9). Yield 48%, white crystals, m.p. 166—168 °C, R_f 0.48 (Silufol, ethyl acetate). Found (%): C, 63.40; H, 5.75; N, 12.48. $C_{18}H_{19}N_3O_2S$. Calculated (%): C, 63.32; H, 5.61; N, 12.31. IR, ν/cm^{-1}: 1682 (C=O). ^{1}H NMR, δ: 1.19 (t, 3 H, N—CH$_2$C<u>H</u>$_3$, J = 7.1 Hz); 2.65 (q, 2 H, N—C<u>H</u>$_2$Me, J = 7.1 Hz); 2.82 (t, 2 H, C(6)H$_2$, J = 5.6 Hz); 3.13 (tt, 2 H, C(5)H$_2$, J = 5.6 Hz, J = 0.9 Hz); 3.71 (t, 2 H, C(8)H$_2$, J = 0.9 Hz); 3.80 (s, 3 H, Ph—OC<u>H</u>$_3$); 7.05—7.09 (m, 2 H, Ph); 7.30 (dd, 1 H, Ph, J = 8.1 Hz, J = 1.7 Hz); 7.45 (dt, 1 H, Ph, J = 8.1 Hz, J = 1.7 Hz); 7.84 (s, 1 H, C(2)H). MS, m/z (I_{rel} (%)): 341 [M]$^+$ (100), 340 (63), 326 (12), 285 (21), 284 (96), 253 (25), 164 (10), 134 (16), 120 (13), 107 (13), 92 (37), 91 (14), 77 (42), 64 (14), 56 (15), 42 (43).

Synthesis of tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidines 8, 10, and 11 (general procedure). *A.* A solution of thieno[2,3-*c*]pyridine **2**—**4** (10 mmol) and triethyl orthoformate (12 mmol) in toluene (50 mL) was refluxed for 1.5—2 h. Then an appropriate aniline (50 mmol) was added and the reaction mixture was refluxed for 36—50 h. The course of the reactions was monitored by TLC. The solvent was removed and the residue was chromatographed on silica gel with ethyl acetate—hexane (1 : 1) as an eluent for tetrahydrothieno[2,3-*c*]pyridines **12**—**14** and with ethyl acetate as an eluent for tetrahydropyrido-[4′,3′:4,5]thieno[2,3-*d*]pyrimidines **8**, **10**, and **11**.

B. Sodium amide (6 mmol) was added at 20 °C to a solution of tetrahydrothieno[2,3-*c*]pyridine **12**—**14** (5 mmol) in toluene (20 mL). The course of the reactions was monitored by TLC. After 24 h, the solvent was removed *in vacuo*. The residue was chromatographed on silica gel with ethyl acetate as an eluent. Tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidines **8**, **10**, and **11** were recrystallized from hexane—ethyl acetate.

Ethyl 6-ethyl-2-[(4-nitrophenyl)aminomethylideneamino]-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (12). Yield 51%, bright yellow crystals turning red when exposed to light, m.p. 136—138 °C, R_f 0.53 (Silufol, ethyl acetate). Found (%): C, 56.82; H, 5.40; N, 13.83. $C_{19}H_{22}N_4O_4S$. Calculated (%): C, 56.70; H, 5.51; N, 13.92. IR, ν/cm^{-1}: 1658 (C=O). ^{1}H NMR, δ: 1.18 (t, 3 H, N—CH$_2$C<u>H</u>$_3$, J = 7.2 Hz); 1.38 (t, 3 H, O—CH$_2$C<u>H</u>$_3$, J = 7.1 Hz); 2.61 (q, 2 H, N—C<u>H</u>$_2$Me, J = 7.2 Hz); 2.75 (t, 2 H, C(4)H$_2$, J = 5.8 Hz); 2.93 (t, 2 H, C(5)H$_2$, J = 5.8 Hz); 3.67 (s, 2 H, C(7)H$_2$); 4.35 (q, 2 H, O—C<u>H</u>$_2$Me, J = 7.1 Hz); 7.15 (d, 2 H, Ph, J = 8.2 Hz); 7.95 (s, 1 H, N=C<u>H</u>—NH); 8.20 (d, 2 H, Ph, J = 8.2 Hz); 11.07 (br.s, 1 H, <u>NH</u>—Ph). MS (DART MS), m/z: 403.1639 [M + H]$^+$.

7-Ethyl-3-(4-nitrophenyl)-5,6,7,8-tetrahydropyrido-[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (8). The yield is 13 (step *A*) and 45% (step *B*), light yellow crystals, m.p. 177—179 °C, R_f 0.45 (Silufol, ethyl acetate). Found (%): C, 57.32; H, 4.71; N, 15.78. $C_{17}H_{16}N_4O_3S$. Calculated (%): C, 57.29; H, 4.52; N, 15.72. IR, ν/cm^{-1}: 1690 (C=O). ^{1}H NMR, δ: 1.20 (t, 3 H, N—CH$_2$C<u>H</u>$_3$, J = 7.0 Hz); 2.66 (q, 2 H, N—C<u>H</u>$_2$Me, J = 7.0 Hz); 2.84 (t, 2 H, C(6)H$_2$, J = 5.5 Hz); 3.13 (tt, 2 H, C(5)H$_2$, J = 5.5 Hz, J = 0.8 Hz); 3.73 (t, 2 H, C(8)H$_2$, J = 0.8 Hz); 7.63 (d, 2 H, Ph, J = 8.7 Hz); 7.98 (s, 1 H, C(2)H); 8.14 (d, 2 H, Ph, J = 8.7 Hz). MS (DART MS), m/z: 357.1259 [M + H]$^+$.

Ethyl 2-anilinomethylideneamino-6-benzyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (13). Yield 57%, yellow oil, R_f 0.63 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 68.75; H, 6.14; N, 9.98. $C_{24}H_{25}N_3O_2S$. Calculated (%): C, 68.71; H, 6.01; N, 10.02. IR, ν/cm^{-1}: 1662 (C=O). ^{1}H NMR, δ: 1.37 (t, 3 H, O—CH$_2$C<u>H</u>$_3$, J = 7.1 Hz); 2.78 (t, 2 H, C(4)H$_2$, J = 5.7 Hz); 2.91 (t, 2 H, C(5)H$_2$, J = 5.7 Hz); 3.56 (s, 2 H, C(7)H$_2$); 3.70 (s, 2 H, C<u>H</u>$_2$Ph); 4.32 (q, 2 H, O—C<u>H</u>$_2$Me, J = 7.1 Hz); 7.06 (d, 2 H, Ph, J = 7.7 Hz); 7.12 (t, 1 H, Ph, J = 7.7 Hz); 7.28 (t, 1 H, Ph, J = 7.1 Hz); 7.31—7.35 (m, 4 H, Ph);

7.38 (d, 2 H, Ph, J = 7.7 Hz); 7.93 (s, 1 H, N=CH—NH); 10.76 (br.s, 1 H, NH—Ph). MS, m/z (I_{rel} (%)): 419 $[M]^+$ (94), 418 (90), 373 (13), 372 (10), 316 (19), 315 (59), 300 (28), 269 (18), 254 (18), 224 (10), 197 (37), 152 (11), 151 (12), 125 (35), 104 (19), 92 (10), 91 (100), 77 (58), 65 (10).

7-Benzyl-3-phenyl-5,6,7,8-tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (10). The yield is 14 (step *A*) and 47% (step *B*), light yellow crystals, m.p. 133—134 °C, R_f 0.51 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 70.53; H, 5.21; N, 11.32. $C_{22}H_{19}N_3OS$. Calculated (%): C, 70.75; H, 5.13; N, 11.25. IR, ν/cm^{-1}: 1682 (C=O). ^{1}H NMR, δ: 2.87 (t, 2 H, C(6)H_2, J = 5.7 Hz); 3.14 (tt, 2 H, C(5)H_2, J = 5.7 Hz, J = 1.7 Hz); 3.70 (t, 2 H, C(8)H_2, J = 1.7 Hz); 3.75 (s, 2 H, CH_2Ph); 7.32—7.40 (m, 7 H, Ph); 7.48—7.56 (m, 3 H, Ph); 7.98 (s, 1 H, C(2)H). MS (DART MS), m/z: 374.09 $[M + H]^+$.

Ethyl 2-anilinomethylideneamino-6-isopropyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (14). Yield 60%, light yellow oil, R_f 0.55 (Silufol, ethyl acetate). Found (%): C, 64.72; H, 6.89; N, 11.25. $C_{20}H_{25}N_3O_2S$. Calculated (%): C, 64.66; H, 6.78; N, 11.31. IR, ν/cm^{-1}: 1687 (C=O). ^{1}H NMR, δ: 1.14 (d, 6 H, N—CH(CH_3)$_2$, J = 6.5 Hz); 1.37 (t, 3 H, O—CH_2CH_3, J = 7.1 Hz); 2.78 (t, 2 H, C(4)H_2, J = 5.8 Hz); 2.88—2.92 (m, 3 H, N—CHMe$_2$, C(5)H_2); 3.65 (s, 2 H, C(7)H_2); 4.33 (q, 2 H, O—CH_2Me, J = 7.1 Hz); 7.07 (d, 2 H, Ph, J = 7.8 Hz); 7.12 (t, 1 H, Ph, J = 7.8 Hz); 7.30 (t, 2 H, Ph, J = 7.8 Hz); 7.93 (s, 1 H, N=CH—NH); 10.79 (br.s, 1 H, NH—Ph). MS (DART MS), m/z: 372.1749 $[M + H]^+$.

7-Isopropyl-3-phenyl-5,6,7,8-tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (11). The yield is 5 (step *A*) and 37% (step *B*), light yellow crystals, m.p. 158—160 °C, R_f 0.48 (Silufol, ethyl acetate). Found (%): C, 66.25; H, 5.95; N, 13.02. $C_{18}H_{19}N_3OS$. Calculated (%): C, 66.43; H, 5.88; N, 12.91. IR, ν/cm^{-1}: 1681 (C=O). ^{1}H NMR, δ: 1.15 (d, 6 H, N—CH(CH_3)$_2$, J = 7.1 Hz); 2.84 (t, 2 H, C(6)H_2, J = 5.7 Hz); 2.97 (sept, 1 H, N—CHMe$_2$, J = 7.1 Hz); 3.11 (tt, 2 H, C(5)H_2, J = 5.7 Hz, J = 1.8 Hz); 3.80 (t, 2 H, C(8)H_2, J = 1.8 Hz); 7.38 (d, 2 H, Ph, J = 8.1 Hz); 7.47 (t, 1 H, Ph, J = 8.1 Hz); 7.52 (t, 2 H, Ph, J = 8.1 Hz); 7.98 (s, 1 H, C(2)H). MS (DART MS), m/z: 326.1347 $[M + H]^+$.

Reactions of tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidines with alkynes (general procedure). A solution of pyridothienopyrimidine **5**—**11** (1 mmol) and DMAD, methyl propiolate, or acetylacetylene (3 mmol) in methanol (30 mL) or acetonitrile (30 mL) was kept at 20 °C or refluxed until the reaction was completed (monitoring by TLC). The solvent was removed and the residue was chromatographed on silica gel. The compounds eluted (in the order of effluence) were 6-methoxymethylthienopyrimidines **19a**—**c**, azocines **16a**—**l***, and spiro compounds **15a**—**l**. The products obtained from compound **5** and DMAD in CH_2Cl_2 were eluted in the following order: thienopyrimidine **18**, pyridothienopyrimidine **17**, and spiro compound **15a**. Compounds **15**—**19** were recrystallized from hexane—ethyl acetate.

Dimethyl 1-methyl-6′-methylidene-4′-oxo-3′-phenyl-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidine]-2,3-dicarboxylate (15a). The yield was 25 (the reaction in MeCN) and 11% (in CH_2Cl_2), colorless crystals, m.p. 216—218 °C, R_f 0.65 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 60.27; H, 4.70; N, 9.54. $C_{22}H_{21}N_3O_5S$. Calculated (%): C, 60.12; H, 4.82; N, 9.56. IR, ν/cm^{-1}: 1696, 1671, 1624 (C=O). ^{1}H NMR, δ: 1.89 (dt, 1 H, C(5)H, J = 13.3 Hz, J = 3.6 Hz); 2.35 (ddd, 1 H, C(5)H, J = 4.2 Hz, J = 11.7 Hz, J = 13.3 Hz); 2.91 (s, 3 H, N—Me); 3.16 (dt, 1 H, C(6)H, J = 12.6 Hz, J = 4.2 Hz); 3.46 (ddd, 1 H, C(6)H, J = 3.6 Hz, J = 11.7 Hz, J = 12.6 Hz); 3.51 (s, 3 H, CO_2Me); 3.85 (s, 3 H, CO_2Me); 5.24 (d, 1 H, =CH, J = 1.6 Hz); 5.30 (d, 1 H, =CH, J = 1.6 Hz); 7.32 (d, 2 H, Ph, J = 8.2 Hz); 7.43 (t, 1 H, Ph, J = 8.2 Hz); 7.48 (t, 2 H, Ph, J = 8.2 Hz); 8.02 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 30.3, 39.8, 44.1, 50.9, 52.5, 52.6, 95.3, 108.5, 125.3, 126.9, 129.1 (2 C), 129.4 (2 C), 136.6, 149.8, 150.3, 151.9, 154.8, 164.4, 165.9, 166.0. MS, m/z (I_{rel} (%)): 439 $[M]^+$ (73), 382 (29), 381 (26), 380 (100), 379 (24), 352 (19), 350 (36), 349 (24), 348 (30), 337 (30), 320 (41), 279 (28), 267 (21), 255 (18), 254 (72), 253 (31), 160 (29), 104 (55), 77 (55).

Dimethyl 1-ethyl-6′-methylidene-4′-oxo-3′-phenyl-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidine]-2,3-dicarboxylate (15b). Yield 18%, white crystals, m.p. 163—164 °C, R_f 0.56 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 61.05; H, 5.24; N, 9.15. $C_{23}H_{23}N_3O_5S$. Calculated (%): C, 60.91; H, 5.11; N, 9.27. IR, ν/cm^{-1}: 1747, 1678 (C=O). ^{1}H NMR, δ: 1.18 (t, 3 H, J = 7.1 Hz, N—CH_2CH_3); 1.89 (td, 1 H, C(5)H, J = 13.1 Hz, J = 3.3 Hz); 2.32 (ddd, 1 H, C(5)H, J = 13.1 Hz, J = 11.6 Hz, J = 4.2 Hz); 3.10—3.22 (m, 3 H, C(6)H, N—CH_2Me); 3.48—3.55 (m, 4 H, C(6)H, CO_2Me); 3.79 (s, 3 H, CO_2Me); 5.16 (d, 1 H, =CH, J = 1.4 Hz); 5.24 (d, 1 H, =CH, J = 1.4 Hz); 7.31 (d, 2 H, Ph, J = 8.1 Hz); 7.40—7.49 (m, 3 H, Ph); 8.01 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 13.7, 29.9, 40.8, 48.1, 51.0, 52.7, 53.0, 94.9, 108.8, 125.6, 127.0 (2 C), 129.2, 129.5 (2 C), 136.8, 149.9, 150.0, 151.9, 154.8, 164.3, 166.0, 166.1. MS, m/z (I_{rel} (%)): 453 $[M]^+$ (20), 394 (18), 388 (17), 381 (13), 380 (93), 362 (95), 361 (15), 333 (21), 306 (10), 280 (13), 279 (23), 278 (10), 245 (10), 207 (14), 104 (64), 91 (11), 77 (100), 69 (12), 59 (35), 44 (22).

Dimethyl 3′-(4-chlorophenyl)-1-ethyl-6′-methylidene-4′-oxo-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidine]-2,3-dicarboxylate (15c). The yield was 44 (the reaction in MeCN) and 24% (in MeOH), light yellow crystals, m.p. 172—174 °C, R_f 0.44 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 56.68; H, 4.37; N, 8.79. $C_{23}H_{22}ClN_3O_5S$. Calculated (%): C, 56.61; H, 4.54; N, 8.61. IR, ν/cm^{-1}: 1745, 1679 (C=O). ^{1}H NMR, δ: 1.19 (t, 3 H, N—CH_2CH_3, J = 7.1 Hz); 1.88 (td, 1 H, C(5)H, J = 13.2 Hz, J = 3.5 Hz); 2.29 (ddd, 1 H, C(5)H, J = 13.2 Hz, J = 11.9 Hz, J = 4.4 Hz); 3.12—3.23 (m, 3 H, C(6)H, N—CH_2Me); 3.48—3.55 (m, 4 H, C(6)H, CO_2Me); 3.86 (s, 3 H, CO_2Me); 5.23 (d, 1 H, =CH, J = 1.8 Hz); 5.31 (d, 1 H, =CH, J = 1.8 Hz); 7.27 (d, 2 H, Ph, J = 8.7 Hz); 7.45 (d, 2 H, Ph, J = 8.7 Hz); 7.98 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 13.6, 30.0, 40.8, 48.0, 50.9, 52.6, 52.9, 108.8, 125.5, 128.3 (2 C), 129.6 (2 C), 135.1, 135.3, 144.9, 149.3, 150.0, 151.7, 154.6, 164.5, 165.9, 166.0. MS (DART MS), m/z: 488.09 $[M + H]^+$.

Methyl 3′-(4-chlorophenyl)-1-ethyl-6′-methylidene-4′-oxo-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidine]-3-carboxylate (15d). The yield was 57 (the reaction in MeCN) and 62% (in MeOH), white crystals, m.p. 199—200 °C, R_f 0.45 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 58.71; H, 4.73; N, 9.76. $C_{21}H_{20}ClN_3O_3S$. Calculated (%): C, 58.67; H, 4.69; N, 9.77. IR, ν/cm^{-1}: 1674, 1616 (C=O). ^{1}H NMR, δ: 1.20 (t, 3 H, N—CH_2CH_3, J = 7.2 Hz); 1.85 (td, 1 H, C(5)H, J = 13.1 Hz, J = 3.4 Hz); 2.29 (ddd, 1 H, C(5)H,

* Compounds **16a**,**h** were not isolated in the individual state; they were detected in the reaction mixtures by ^{1}H NMR spectroscopy.

J = 13.1 Hz, *J* = 11.7 Hz, *J* = 4.7 Hz); 3.07—3.09 (m, 1 H, C(6)H); 3.25 (q, 2 H, N—C$\underline{H}_2$Me, *J* = 7.2 Hz); 3.39 (ddd, 1 H, C(6)H, *J* = 12.9 Hz, *J* = 11.7 Hz, *J* = 3.4 Hz); 3.56 (s, 3 H, CO_2Me); 5.15 (d, 1 H, =CH, *J* = 2.0 Hz); 5.29 (d, 1 H, =CH, *J* = 2.0 Hz); 7.29 (d, 2 H, Ph, *J* = 8.7 Hz); 7.43 (d, 2 H, Ph, *J* = 8.7 Hz); 7.65 (s, 1 H, C(2)H); 7.99 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 13.7, 30.4, 39.5, 50.3, 50.6, 52.3, 108.0, 125.3, 128.1 (2 C), 129.4 (2 C), 135.0 (2 C), 144.9, 146.3, 149.1, 152.4, 154.7, 164.8, 166.6. MS (DART MS), *m/z*: 430.09 $[M + H]^+$.

3-Acetyl-3′-(4-chlorophenyl)-1-ethyl-6′-methylidene-5,6-dihydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidin]-4′(3′*H*)-one (15e). Yield 37%, white crystals, m.p. 232—234 °C, R_f 0.50 (Sorbfil, ethyl acetate). Found (%): C, 60.78; H, 4.95; N, 10.12. $C_{21}H_{20}ClN_3O_2S$. Calculated (%): C, 60.94; H, 4.87; N, 10.15. IR, ν/cm^{-1}: 1674 (C=O). ^{1}H NMR, δ: 1.25 (t, 3 H, N—$CH_2C\underline{H}_3$, *J* = 7.2 Hz); 1.85 (td, 1 H, C(5)H, *J* = 13.2 Hz, *J* = 3.6 Hz); 2.11 (s, 3 H, COMe); 2.26 (ddd, 1 H, C(5)H, *J* = 13.2 Hz, *J* = 11.9 Hz, *J* = 4.5 Hz); 3.12—3.14 (m, 1 H, C(6)H); 3.30 (q, 2 H, N—C$\underline{H}_2$Me, *J* = 7.2 Hz); 3.43 (ddd, 1 H, C(6)H, *J* = 12.6 Hz, *J* = 11.9 Hz, *J* = 3.6 Hz); 5.02 (d, 1 H, =CH, *J* = 1.5 Hz); 5.22 (d, 1 H, =CH, *J* = 1.5 Hz); 7.29 (d, 2 H, Ph, *J* = 8.7 Hz); 7.43 (d, 2 H, Ph, *J* = 8.7 Hz); 7.47 (s, 1 H, C(2)H); 7.96 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 13.8, 24.1, 30.4, 39.8, 51.0, 52.2, 106.9, 125.7, 128.2 (2 C), 129.4 (2 C), 135.0, 135.2, 144.9, 147.7, 148.9, 152.4, 154.7, 164.8, 191.0. MS (DART MS), *m/z*: 414.1023 $[M + H]^+$.

Dimethyl 1-ethyl-6′-methylidene-3′-(4-nitrophenyl)-4′-oxo-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidine]-2,3-dicarboxylate (15f). The yield was 28 (the reaction in MeCN) and 17% (in MeOH), light yellow crystals, m.p. 209—211 °C. R_f 0.40 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 55.23; H, 4.53; N, 11.31. $C_{23}H_{22}N_4O_7S$. Calculated (%): C, 55.41; H, 4.45; N, 11.24. IR, ν/cm^{-1}: 1740, 1678 (C=O). ^{1}H NMR, δ: 1.20 (t, 3 H, N—$CH_2C\underline{H}_3$, *J* = 6.9 Hz); 1.90 (td, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 3.4 Hz); 2.28 (ddd, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 12.3 Hz, *J* = 4.1 Hz); 3.15—3.23 (m, 3 H, C(6)H, N—C$\underline{H}_2$Me); 3.48—3.55 (m, 4 H, C(6)H, CO_2Me); 3.86 (s, 3 H, CO_2CH_3); 5.25 (d, 1 H, =CH, *J* = 2.0 Hz); 5.33 (d, 1 H, =CH, *J* = 2.0 Hz); 7.57 (d, 2 H, Ph, *J* = 8.9 Hz); 8.02 (s, 1 H, C(2′)H); 8.34 (d, 2 H, Ph, *J* = 8.9 Hz). ^{13}C NMR, δ: 13.6, 29.9, 40.6, 48.1, 51.0, 52.8, 94.5, 109.2, 124.7 (2 C), 125.6, 128.1 (2 C), 141.8, 147.7, 148.6, 148.7, 150.0, 151.3, 154.0, 165.0, 165.8, 166.0. MS (DART MS), *m/z*: 499.1277 $[M + H]^+$.

Methyl 1-ethyl-6′-methylidene-3′-(4-nitrophenyl)-4′-oxo-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidine]-3-carboxylate (15g). The yield was 25 (the reaction in MeCN) and 51% (in MeOH), yellow crystals, m.p. 218—220 °C, R_f 0.47 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 57.17; H, 4.63; N, 12.81. $C_{21}H_{20}N_4O_5S$. Calculated (%): C, 57.26; H, 4.58; N, 12.72. IR, ν/cm^{-1}: 1668, 1614 (C=O). ^{1}H NMR, δ: 1.22 (t, 3 H, N—$CH_2C\underline{H}_3$, *J* = 7.1 Hz); 1.89 (td, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 3.5 Hz); 2.28 (ddd, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 11.9 Hz, *J* = 4.5 Hz); 3.10 (dt, 1 H, C(6)H, *J* = 12.4 Hz, *J* = 4.5 Hz); 3.22—3.32 (m, 2 H, N—C$\underline{H}_2$Me); 3.42 (ddd, 1 H, C(6)H, *J* = 12.4 Hz, *J* = 11.9 Hz, *J* = 3.5 Hz); 3.58 (s, 3 H, CO_2Me); 5.18 (d, 1 H, =CH, *J* = 1.3 Hz); 5.32 (d, 1 H, =CH, *J* = 1.3 Hz); 7.59 (d, 2 H, Ph, *J* = 9.0 Hz); 7.67 (s, 1 H, C(2)H); 8.03 (s, 1 H, C(2′)H); 8.34 (d, 2 H, Ph, *J* = 9.0 Hz). ^{13}C NMR, δ: 13.9, 30.4, 39.6, 50.5, 50.8, 52.6, 95.9, 108.5, 124.7 (2 C), 125.6, 128.1 (2 C), 142.0, 146.4, 147.8, 148.6, 152.2, 154.5, 165.4, 166.7. MS (DART MS), *m/z*: 441.1225 $[M + H]^+$.

3-Acetyl-1-ethyl-6′-methylidene-3′-(4-nitrophenyl)-5,6-dihydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]pyrimidin]-4′(3′*H*)-one (15h). Yield 9%, white crystals, m.p. 255—257 °C, R_f 0.54 (Sorbfil, ethyl acetate). Found (%): C, 59.48; H, 4.90; N, 13.19. $C_{21}H_{20}N_4O_4S$. Calculated (%): C, 59.42; H, 4.75; N, 13.20. IR, ν/cm^{-1}: 1674 (C=O). ^{1}H NMR, δ: 1.26 (t, 3 H, N—$CH_2C\underline{H}_3$, *J* = 7.2 Hz); 1.88 (td, 1 H, C(5)H, *J* = 13.3 Hz, *J* = 3.5 Hz); 2.13 (s, 3 H, COMe); 2.25 (ddd, 1 H, C(5)H, *J* = 13.3 Hz, *J* = 11.7 Hz, *J* = 4.5 Hz); 3.14 (dt, 1 H, C(6)H, *J* = 12.7 Hz, *J* = 4.5 Hz); 3.29—3.36 (m, 2 H, N—C$\underline{H}_2$Me); 3.46 (ddd, 1 H, C(6)H, *J* = 12.7 Hz, *J* = 11.7 Hz, *J* = 3.5 Hz); 5.04 (d, 1 H, =CH, *J* = 1.2 Hz); 5.24 (d, 1 H, =CH, *J* = 1.2 Hz); 7.49 (s, 1 H, C(2)H); 7.57 (d, 2 H, Ph, *J* = 8.8 Hz); 8.00 (s, 1 H, C(2′)H); 8.33 (d, 2 H, Ph, *J* = 8.8 Hz). ^{13}C NMR, δ: 13.8, 24.1, 30.2, 39.7, 51.1, 52.3, 107.3, 110.2, 124.6 (2 C), 126.0, 128.0 (2 C), 142.0, 147.8 (2 C), 148.1, 152.1, 154.2, 165.2, 191.0. MS (DART MS), *m/z*: 425.1389 $[M + H]^+$.

Dimethyl 1-ethyl-3′-(2-methoxyphenyl)-6′-methylidene-4′-oxo-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]-pyrimidine]-2,3-dicarboxylate (15i). The yield was 45 (the reaction in MeCN) and 50% (in MeOH), colorless crystals, m.p. 177—179 °C, R_f 0.67 (Sorbfil, ethyl acetate). Found (%): C, 59.75; H, 5.32; N, 8.55. $C_{24}H_{25}N_3O_6S$. Calculated (%): C, 59.61; H, 5.21; N, 8.69. IR, ν/cm^{-1}: 1737, 1685, 1678 (C=O). ^{1}H NMR, δ: 1.18 (t, 3 H, N—$CH_2C\underline{H}_3$, *J* = 6.9 Hz); 1.88 (td, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 3.1 Hz); 2.30 (ddd, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 12.5 Hz, *J* = 4.3 Hz); 3.11—3.19 (m, 3 H, C(6)H, N—C$\underline{H}_2$Me); 3.48—3.54 (m, 4 H, C(6)H, CO_2Me); 3.78 (s, 3 H, Ph—O$C\underline{H}_3$); 3.85 (s, 3 H, CO_2Me); 5.22 (d, 1 H, =CH, *J* = 1.4 Hz); 5.31 (d, 1 H, =CH, *J* = 1.4 Hz); 7.00—7.04 (m, 2 H, Ph); 7.21—7.26 (m, 1 H, Ph); 7.40 (dt, 1 H, Ph, *J* = 8.3 Hz, *J* = 2.1 Hz); 7.88 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 13.6, 29.9, 40.5, 47.9, 50.7, 52.6, 52.8, 55.9, 94.6, 108.5, 112.1, 120.8, 125.2, 125.7, 129.1, 130.8, 149.9, 150.9, 151.9, 154.4, 154.7, 136.8, 166.1, 166.3. MS, *m/z* (I_{rel} (%)): 483 $[M]^+$ (87), 452 (12), 425 (32), 424 (36), 423 (15), 393 (10), 392 (14), 379 (20), 369 (22), 367 (44), 366 (34), 364 (26), 349 (16), 335 (17), 310 (55), 309 (85), 308 (23), 295 (16), 279 (23), 251 (16), 241 (11), 207 (60), 203 (21), 276 (13), 260 (13), 147 (38), 133 (35), 120 (20), 107 (21), 92 (51), 91 (30), 77 (76), 70 (25), 59 (52), 57 (33), 44 (100).

Methyl 1-ethyl-3′-(2-methoxyphenyl)-6′-methylidene-4′-oxo-3′,4′,5,6-tetrahydro-1*H*-spiro[pyridine-4,5′-thieno[2,3-*d*]-pyrimidine]-3-carboxylate (15j). The yield was 30 (the reaction in MeCN) and 8% (in MeOH), light yellow crystals, m.p. 167—169 °C, R_f 0.28 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 62.17; H, 5.49; N, 9.84. $C_{22}H_{23}N_3O_4S$. Calculated (%): C, 62.10; H, 5.45; N, 9.88. IR, ν/cm^{-1}: 1672, 1611 (C=O). ^{1}H NMR, δ: 1.19 (t, 3 H, N—$CH_2C\underline{H}_3$, *J* = 7.2 Hz); 1.87 (td, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 3.4 Hz); 2.32 (ddd, 1 H, C(5)H, *J* = 13.1 Hz, *J* = 11.8 Hz, *J* = 4.8 Hz); 3.05—3.09 (m, 1 H, C(6)H); 3.23 (q, 2 H, N—C$\underline{H}_2$Me, *J* = 7.2 Hz); 3.39 (ddd, 1 H, C(6)H, *J* = 12.5 Hz, *J* = 11.8 Hz, *J* = 3.4 Hz); 3.56 (s, 3 H, CO_2Me); 3.79 (s, 3 H, Ph—O$C\underline{H}_3$); 5.15 (d, 1 H, =CH, *J* = 1.4 Hz); 5.28 (d, 1 H, =CH, *J* = 1.4 Hz); 7.00—7.03 (m, 2 H, Ph); 7.24—7.26 (m, 1 H, Ph); 7.39 (td, 1 H, Ph, *J* = 8.2 Hz, *J* = 2.0 Hz); 7.63 (s, 1 H, C(2)H); 7.90 (s, 1 H, C(2′)H). ^{13}C NMR, δ: 13.8, 30.6, 39.5, 50.3, 50.5, 52.4, 55.8, 96.2, 107.6, 112.0, 120.7, 125.4, 128.8, 129.3, 130.7, 146.3, 150.9, 152.8, 154.2, 155.1, 164.3, 166.8. MS, *m/z* (I_{rel} (%)): 425 $[M]^+$ (61), 392 (10), 378 (10), 368 (10), 367 (24), 366 (100), 352 (88), 324 (10), 309 (11), 207 (10), 92 (35), 91 (15), 77 (28), 44 (15).

3-Acetyl-1-ethyl-3´-(2-methoxyphenyl)-6´-methylidene-5,6-dihydro-1*H*-spiro[pyridine-4,5´-thieno[2,3-*d*]pyrimidin]-4´(3´*H*)-one (15k). Yield 46%, light yellow crystals, m.p. 194—196 °C, R_f 0.48 (Sorbfil, ethyl acetate). Found (%): C, 64.65; H, 5.58; N, 10.27. $C_{22}H_{23}N_3O_3S$. Calculated (%): C, 64.53; H, 5.66; N, 10.26. IR, ν/cm^{-1}: 1666 (C=O). ^{1}H NMR, δ: 1.22 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.3 Hz); 1.86 (td, 1 H, C(5)H, J = 13.4 Hz, J = 3.4 Hz); 2.09 (s, 3 H, COMe); 2.29 (ddd, 1 H, C(5)H, J = 13.4 Hz, J = 11.9 Hz, J = 4.2 Hz); 3.12 (dt, 1 H, C(6)H, J = 12.9 Hz, J = 4.2 Hz); 3.28 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.3 Hz); 3.42 (ddd, 1 H, C(6)H, J = 12.9 Hz, J = 11.9 Hz, J = 3.4 Hz); 3.78 (s, 3 H, Ph—$OC\underline{H}_3$); 5.02 (d, 1 H, =CH, J = 1.3 Hz); 5.20 (d, 1 H, =CH, J = 1.3 Hz); 6.98—7.02 (m, 2 H, Ph); 7.24—7.28 (m, 1 H, Ph); 7.38 (td, 1 H, Ph, J = 8.1 Hz, J = 1.5 Hz); 7.46 (br.s, 1 H, C(2)H); 7.87 (br.s, 1 H, C(2´)H). ^{13}C NMR, δ: 13.9, 24.4, 29.8, 30.8, 39.9, 51.0, 52.3, 55.9, 106.4, 112.1, 120.9, 125.5, 125.8, 129.2, 130.8, 147.7, 150.6, 152.9, 154.4, 155.1, 164.5, 191.1. MS (DART MS), *m/z*: 410.1528 [M + H]$^+$.

Dimethyl 1-isopropyl-6´-methylidene-4´-oxo-3´-phenyl-3´,4´,5,6-tetrahydro-1*H*-spiro[pyridine-4,5´-thieno[2,3-*d*]pyrimidine]-2,3-dicarboxylate (15l). Yield 57%, colorless crystals, m.p. 139—140 °C, R_f 0.60 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 61.46; H, 5.48; N, 9.09. $C_{24}H_{25}N_3O_5S$. Calculated (%): C, 61.65; H, 5.39; N, 8.99. IR, ν/cm^{-1}: 1734, 1679 (C=O). ^{1}H NMR, δ: 1.19 (d, 3 H, N—CHC$\underline{H}_3$, J = 6.4 Hz); 1.21 (d, 3 H, N—CHC$\underline{H}_3$, J = 6.4 Hz); 1.88 (td, 1 H, C(5)H, J = 13.1 Hz, J = 3.3 Hz); 2.22 (ddd, 1 H, C(5)H, J = 13.1 Hz, J = 10.9 Hz, J = 5.5 Hz); 3.23—3.32 (m, 2 H, C(6)H_2); 3.51 (s, 3 H, CO_2Me); 3.59—3.66 (m, 1 H, N—C$\underline{H}$Me$_2$); 3.85 (s, 3 H, CO_2Me); 5.23 (d, 1 H, =CH, J = 1.7 Hz); 5.30 (d, 1 H, =CH, J = 1.7 Hz); 7.31 (d, 2 H, Ph, J = 8.1 Hz); 7.42—7.50 (m, 3 H, Ph); 8.00 (s, 1 H, C(2´)H). ^{13}C NMR, δ: 20.2, 20.4, 29.9, 33.7, 50.8, 52.2, 52.6, 94.8, 108.7, 125.6, 126.9 (2 C), 129.1, 129.4 (2 C), 136.7, 147.3, 149.7, 150.2, 152.0, 154.7, 164.2, 166.2, 166.3. MS (DART MS), *m/z*: 468.1612 [M + H]$^+$.

Dimethyl 7-ethyl-4-oxo-3-phenyl-3,4,5,6,7,10-hexahydropyrimido[5´,4´:4,5]thieno[3,2-*d*]azocine-8,9-dicarboxylate (16b). Yield 6%, white crystals, m.p. 183—184 °C, R_f 0.63 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 60.94; H, 5.26; N, 9.38. $C_{23}H_{23}N_3O_5S$. Calculated (%): C, 60.91; H, 5.11; N, 9.27. IR, ν/cm^{-1}: 1727, 1677 (C=O). ^{1}H NMR, δ: 1.04 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.1 Hz); 3.03 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.1 Hz); 3.69—3.73 (m, 5 H, C(5)H_2, CO_2Me); 3.79 (s, 3 H, CO_2Me); 3.87 (t, 2 H, C(6)H_2, J = 6.5 Hz); 4.10 (s, 2 H, C(10)H_2); 7.37 (d, 2 H, Ph, J = 7.1 Hz); 7.46—7.55 (m, 3 H, Ph); 7.99 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.1, 26.8, 28.0, 46.0, 48.7, 51.7, 52.5, 123.3, 127.2 (2 C), 129.2, 129.6 (2 C), 131.3, 134.8, 137.1, 145.4, 154.2, 156.2, 157.9, 161.8, 167.2, 168.4. MS (DART MS), *m/z*: 454.12 [M + H]$^+$.

Dimethyl 3-(4-chlorophenyl)-7-ethyl-4-oxo-3,4,5,6,7,10-hexahydropyrimido[5´,4´:4,5]thieno[3,2-*d*]azocine-8,9-dicarboxylate (16c). The yield was 14 (the reaction in MeCN) and 6% (in MeOH), white crystals, m.p. 213—215 °C, R_f 0.63 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 56.70; H, 4.57; N, 8.57. $C_{23}H_{22}ClN_3O_5S$. Calculated (%): C, 56.61; H, 4.54; N, 8.61. IR, ν/cm^{-1}: 1740, 1675 (C=O). ^{1}H NMR, δ: 1.04 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.1 Hz); 3.04 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.1 Hz); 3.68—3.71 (m, 5 H, C(5)H_2, CO_2Me); 3.80 (s, 3 H, CO_2Me); 3.87 (t, 2 H, C(6)H_2, J = 6.4 Hz); 4.10 (s, 2 H, C(10)H_2); 7.33 (d, 2 H, Ph, J = 8.7 Hz); 7.51 (d, 2 H, Ph, J = 8.7 Hz); 7.95 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.1, 26.8, 28.1, 46.1, 48.7, 51.8, 52.5, 123.2, 128.5 (2 C), 129.8 (2 C), 131.3, 135.1, 135.4, 135.5, 144.9, 154.1, 157.7, 161.8, 167.1, 168.4, 168.8. MS (DART MS), *m/z*: 488.05 [M + H]$^+$.

Methyl 3-(4-chlorophenyl)-7-ethyl-4-oxo-3,4,5,6,7,10-hexahydropyrimido[5´,4´:4,5]thieno[3,2-*d*]azocine-9-carboxylate (16d). Yield 11% (the reaction in MeOH), white crystals, m.p. 275—278 °C, R_f 0.57 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 58.39; H, 4.82; N, 9.68. $C_{21}H_{20}ClN_3O_3S$. Calculated (%): C, 58.67; H, 4.69; N, 9.77. IR, ν/cm^{-1}: 1688, 1665, 1617 (C=O). ^{1}H NMR, δ: 1.19 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.3 Hz); 3.22 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.3 Hz); 3.64 (t, 2 H, C(5)H_2, J = 5.8 Hz); 3.70 (s, 3 H, CO_2Me); 3.89—3.94 (m, 2 H, C(6)H_2); 4.10 (s, 2 H, C(10)H_2); 7.32 (d, 2 H, Ph, J = 8.6 Hz); 7.48 (s, 1 H, C(8)H); 7.50 (d, 2 H, Ph, J = 8.6 Hz); 7.93 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.9, 24.6, 31.8, 45.7, 51.2, 51.9, 93.7, 124.0, 128.6 (2 C), 129.7 (2 C), 129.9, 135.3, 135.6, 136.8, 144.9, 149.9, 157.8, 161.1, 169.7. MS (DART MS), *m/z*: 430.0997 [M + H]$^+$.

9-Acetyl-3-(4-chlorophenyl)-7-ethyl-5,6,7,10-tetrahydropyrimido[5´,4´:4,5]thieno[3,2-*d*]azocin-4(3*H*)-one (16e). Yield 7%, white crystals, m.p. 285—287 °C, R_f 0.78 (Sorbfil, ethyl acetate). Found (%): C, 61.07; H, 4.92; N, 10.23. $C_{21}H_{20}ClN_3O_2S$. Calculated (%): C, 60.94; H, 4.87; N, 10.15. IR, ν/cm^{-1}: 1690, 1609 (C=O). ^{1}H NMR, δ: 1.24 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.2 Hz); 2.21 (s, 3 H, COMe); 3.28 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.2 Hz); 3.66 (t, 2 H, C(5)H_2, J = 5.8 Hz); 3.94—4.00 (m, 2 H, C(6)H_2); 4.19 (s, 2 H, C(10)H_2); 7.30—7.32 (m, 3 H, Ph, C(8)H); 7.50 (d, 2 H, Ph, J = 8.7 Hz); 7.92 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.9, 22.5, 24.7, 31.5, 45.9, 52.2, 108.3, 123.8, 128.5 (2 C), 129.7 (2 C), 135.3, 135.6, 137.0, 144.9, 151.7, 157.8, 161.2, 182.0, 193.3. MS (DART MS), *m/z*: 414.1026 [M + H]$^+$.

Dimethyl 7-ethyl-3-(4-nitrophenyl)-4-oxo-3,4,5,6,7,10-hexahydropyrimido[5´,4´:4,5]thieno[3,2-*d*]azocine-8,9-dicarboxylate (16f). The yield was 12 (the reaction in MeCN) and 14% (in MeOH), yellow crystals, m.p. 208—210 °C, R_f 0.55 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 55.65; H, 4.52; N, 11.32. $C_{23}H_{22}N_4O_7S$. Calculated (%): C, 55.41; H, 4.45; N, 11.24. IR, ν/cm^{-1}: 1739, 1678 (C=O). ^{1}H NMR, δ: 1.05 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.2 Hz); 3.04 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.2 Hz); 3.69 (t, 2 H, C(5)H_2, J = 6.5 Hz); 3.71 (s, 3 H, CO_2Me); 3.81 (s, 3 H, CO_2Me); 3.89 (t, 2 H, C(6)H_2, J = 6.5 Hz); 4.11 (s, 2 H, C(10)H_2); 7.62 (d, 2 H, Ph, J = 8.9 Hz); 7.97 (s, 1 H, C(2)H); 8.41 (d, 2 H, Ph, J = 8.9 Hz). ^{13}C NMR, δ: 14.1, 26.7, 28.1, 46.1, 48.4, 51.9, 52.7, 123.1, 124.9 (2 C), 128.4 (2 C), 131.3, 135.6, 142.3, 143.9, 144.0, 147.8, 154.1, 157.2, 161.6, 167.1, 168.4. MS (DART MS), *m/z*: 499.1293 [M + H]$^+$.

Methyl 7-ethyl-3-(4-nitrophenyl)-4-oxo-3,4,5,6,7,10-hexahydropyrimido[5´,4´:4,5]thieno[3,2-*d*]azocine-9-carboxylate (16g). The yield was 9 (the reaction in MeCN) and 3% (in MeOH), light yellow crystals, m.p. 219—221 °C, R_f 0.58 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 57.48; H, 4.64; N, 12.80. $C_{21}H_{20}N_4O_5S$. Calculated (%): C, 57.29; H, 4.58; N, 12.72. IR, ν/cm^{-1}: 1680, 1621 (C=O). ^{1}H NMR, δ: 1.20 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.2 Hz); 3.23 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.2 Hz); 3.64 (t, 2 H, C(5)H_2, J = 5.6 Hz); 3.70 (s, 3 H, CO_2Me); 3.90—3.95 (m, 2 H, C(6)H_2); 4.11 (s, 2 H, C(10)H_2); 7.49 (s, 1 H, C(8)H); 7.61 (d, 2 H, Ph, J = 8.8 Hz); 7.96 (s, 1 H, C(2)H); 8.41 (d, 2 H, Ph, J = 8.8 Hz). ^{13}C NMR, δ: 15.0, 24.7, 32.0, 45.8, 51.3, 52.0, 93.8, 124.0, 124.9 (2 C), 128.4 (2 C), 130.2, 137.5, 142.6, 144.1, 147.9, 150.0, 157.4, 161.2, 169.8. MS (DART MS), *m/z*: 441.1244 [M + H]$^+$.

Dimethyl 7-ethyl-3-(2-methoxyphenyl)-4-oxo-3,4,5,6,7,10-hexahydropyrimido[5′,4′:4,5]thieno[3,2-*d*]azocine-8,9-dicarboxylate (16i). Yield 18% (the reaction in MeCN), white crystals, m.p. 187—189 °C, R_f 0.40 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 59.63; H, 5.32; N, 8.67. $C_{24}H_{25}N_3O_6S$. Calculated (%): C, 59.61; H, 5.21; N, 8.69. IR, ν/cm^{-1}: 1736, 1678 (C=O). ^{1}H NMR, δ: 1.03 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.3 Hz); 3.04 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.3 Hz); 3.70—3.72 (m, 5 H, C(5)H_2, CO_2Me); 3.80 (s, 6 H, CO_2Me, Ph—$OC\underline{H}_3$); 3.87 (t, 2 H, C(6)H_2, J = 6.3 Hz); 4.09 (s, 2 H, C(10)H_2); 7.06—7.10 (m, 2 H, Ph); 7.29 (dd, 1 H, Ph, J = 8.1 Hz, J = 1.9 Hz); 7.46 (dt, 1 H, Ph, J = 8.1 Hz, J = 1.9 Hz); 7.85 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.1, 26.7, 28.0, 46.0, 48.8, 51.7, 52.5, 55.8, 97.2, 112.2, 120.9, 123.5, 125.6, 129.1, 131.0, 131.2, 134.1, 146.5, 151.2, 151.6, 157.9, 161.8, 167.2, 168.5. MS, m/z (I_{rel} (%)): 483 [M]$^+$ (10), 412 (10), 380 (11), 349 (10), 335 (24), 309 (97), 308 (42), 291 (19), 279 (19), 278 (100), 277 (21), 251 (10), 211 (10), 208 (10), 207 (45), 205 (10), 203 (41), 191 (10), 186 (11), 147 (17), 133 (20), 120 (16), 105 (15), 97 (19), 92 (31), 77 (50), 70 (24), 63 (37), 55 (36), 53 (28), 44 (79), 43 (42).

Methyl 7-ethyl-3-(2-methoxyphenyl)-4-oxo-3,4,5,6,7,10-hexahydropyrimido[5′,4′:4,5]thieno[3,2-*d*]azocine-9-carboxylate (16j). Yield 12% (the reaction in MeCN), white crystals, m.p. 195—197 °C, R_f 0.61 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 62.12; H, 5.52; N, 9,87. $C_{22}H_{23}N_3O_4S$. Calculated (%): C, 62.10; H, 5.45; N, 9.88. IR, ν/cm^{-1}: 1678, 1658, 1612 (C=O). ^{1}H NMR, δ: 1.19 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.2 Hz); 3.22 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.2 Hz); 3.64—3.66 (m, 2 H, C(5)H_2); 3.69 (s, 3 H, Ph—$OC\underline{H}_3$); 3.80 (s, 3 H, CO_2Me); 3.90—3.93 (m, 2 H, C(6)H_2); 4.09 (s, 2 H, C(10)H_2); 7.05—7.09 (m, 2 H, Ph); 7.28 (dd, 1 H, Ph, J = 8.1 Hz, J = 1.9 Hz); 7.45 (dt, 1 H, Ph, J = 8.1 Hz, J = 1.9 Hz); 7.49 (s, 1 H, C(8)H); 7.83 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.8, 24.5, 31.8, 45.7, 51.2, 51.8, 55.8, 93.7, 112.1, 120.8, 124.3, 125.6, 129.2, 129.9, 130.9, 135.8, 146.5, 149.9, 154.6, 157.9, 161.1, 169.7. MS (DART MS), m/z: 426.1546 [M + H]$^+$.

9-Acetyl-7-ethyl-3-(2-methoxyphenyl)-5,6,7,10-tetrahydropyrimido[5′,4′:4,5]thieno[3,2-*d*]azocin-4(3*H*)-one (16k). Yield 10%, white crystals, m.p. 211—213 °C, R_f 0.47 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 64.69; H, 5.78; N, 10.14. $C_{22}H_{23}N_3O_3S$. Calculated (%): C, 64.53; H, 5.66; N, 10.26. IR, ν/cm^{-1}: 1675 (C=O). ^{1}H NMR, δ: 1.23 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 7.2 Hz); 2.21 (s, 3 H, COMe); 3.28 (q, 2 H, N—$C\underline{H}_2$Me, J = 7.2 Hz); 3.66—3.70 (m, 2 H, C(5)H_2); 3.80 (s, 3 H, Ph—$OC\underline{H}_3$); 3.92—3.99 (m, 2 H, C(6)H_2); 4.09 (br.s, 2 H, C(10)H_2); 7.06—7.09 (m, 2 H, Ph); 7.28 (dd, 1 H, Ph, J = 7.7 Hz, J = 1.4 Hz); 7.32 (s, 1 H, C(8)H); 7.46 (dt, 1 H, Ph, J = 7.7 Hz, J = 1.4 Hz); 7.82 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.9, 22.6, 24.8, 31.6, 46.1, 52.3, 55.9, 108.5, 112.3, 121.0, 124.3, 125.7, 129.3, 129.9, 131.0, 136.2, 146.6, 151.9, 154.8, 158.0, 161.4, 193.4. MS (DART MS), m/z: 410.1531 [M + H]$^+$.

Dimethyl 7-isopropyl-4-oxo-3-phenyl-3,4,5,6,7,10-hexahydropyrimido[5′,4′:4,5]thieno[3,2-*d*]azocine-8,9-dicarboxylate (16l). Yield 11%, white crystals, m.p. 177—178 °C, R_f 0.68 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 61.57; H, 5.53; N, 8.78. $C_{24}H_{25}N_3O_5S$. Calculated (%): C, 61.65; H, 5.39; N, 8.99. IR, ν/cm^{-1}: 1736, 1678 (C=O). ^{1}H NMR, δ: 1.13 (d, 6 H, N—$CH(C\underline{H}_3)_2$, J = 6.6 Hz); 3.47 (sept, 1 H, N—$C\underline{H}Me_2$, J = 6.6 Hz); 3.67—3.70 (m, 5 H, C(5)H_2, CO_2Me); 3.81 (s, 3 H, CO_2Me); 3.83 (t, 2 H, C(6)H_2, J = 6.2 Hz); 4.03 (s, 2 H, C(10)H_2); 7.36 (d, 2 H, Ph, J = 7.4 Hz); 7.48—7.55 (m, 3 H, Ph); 7.98 (s, 1 H, C(2)H). ^{13}C NMR, δ: 21.0 (2 C), 26.5, 29.3, 44.5, 51.6, 52.5, 53.0, 123.0, 127.2 (2 C), 129.2, 129.5 (2 C), 129.7, 132.5, 134.8, 137.2, 145.3, 154.0, 157.9, 161.5, 167.5, 168.3. MS (DART MS), m/z: 468.1740 [M + H]$^+$.

Dimethyl (2*E*)-2-(4-oxo-3-phenyl-3,5,6,8-tetrahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-7(4*H*)-yl)but-2-enedioate (17). Yield 11%, white crystals, m.p. 196—198 °C, R_f 0.77 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 59.12; H, 4.69; N, 10.00. $C_{21}H_{19}N_3O_5S$. Calculated (%): C, 59.28; H, 4.50; N, 9.88. IR, ν/cm^{-1}: 1737, 1688 (C=O). ^{1}H NMR, δ: 3.21 (tt, 2 H, C(5)H_2, J = 5.7 Hz, J = 1.6 Hz); 3.51 (t, 2 H, C(6)H_2, J = 5.7 Hz); 3.66 (s, 3 H, CO_2Me); 3.97 (s, 3 H, CO_2Me); 4.40 (t, 2 H, C(8)H_2, J = 1.6 Hz); 4.88 (s, 1 H, =CH—); 7.37—7.39 (m, 2 H, Ph); 7.50—7.54 (m, 3 H, Ph); 8.03 (s, 1 H, C(2)H). ^{13}C NMR, δ: 25.5, 45.3, 46.1, 50.9, 53.1, 87.4, 127.0 (2 C), 128.7, 129.3, 129.6 (2 C), 129.7, 130.5, 136.7, 146.1, 153.9, 157.2, 162.9, 165.7, 167.6. MS (DART MS), m/z: 426.1090 [M + H]$^+$.

Dimethyl (2*E*)-2-{[2-(6-hydroxymethyl-4-oxo-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidin-5-yl)ethyl](*N*-methyl)amino}but-2-enedioate (18). Yield 1%, white crystals, m.p. 150—152 °C, R_f 0.48 (Sorbfil, ethyl acetate—hexane, 1 : 2). Found (%): C, 57.82; H, 5.15; N, 9.16. $C_{22}H_{23}N_3O_6S$. Calculated (%): C, 57.76; H, 5.07; N, 9.18. IR, ν/cm^{-1}: 1736, 1693 (C=O). ^{1}H NMR, δ: 1.52 (s, 1 H, OH); 2.88 (s, 3 H, N—Me); 3.27—3.31 (m, 2 H, C(β)H_2); 3.39—3.43 (m, 2 H, C(α)H_2); 3.64 (s, 3 H, CO_2Me); 3.94 (s, 3 H, CO_2Me); 4.64 (s, 1 H, =CH—); 4.84 (s, 2 H, $C\underline{H}_2$OH); 7.38—7.40 (m, 2 H, Ph); 7.52—7.59 (m, 3 H, Ph); 8.06 (s, 1 H, C(2)H). ^{13}C NMR, δ: 26.6, 37.6, 42.9, 45.3, 50.8, 53.2, 84.7, 126.0, 127.1 (2 C), 128.8, 129.0, 129.8 (2 C), 132.0, 133.8, 146.2, 146.8, 154.5, 166.2, 168.8, 169.0. MS (DART MS), m/z: 476.09 [M + H_3O]$^+$.

Dimethyl (2*E*)-2-({2-[3-(4-chlorophenyl)-6-methoxymethyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-5-yl]ethyl}(ethyl)amino)but-2-enedioate (19a). Yield 7%, white crystals, m.p. 173—175 °C, R_f 0.69 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 55.45; H, 5.12; N, 8.08. $C_{24}H_{26}ClN_3O_6S$. Calculated (%): C, 55.43; H, 5.04; N, 8.08. IR, ν/cm^{-1}: 1725, 1696, 1675 (C=O). ^{1}H NMR, δ: 1.12 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 6.9 Hz); 3.17—3.25 (m, 4 H, N—$C\underline{H}_2$Me, C(α)H_2); 3.35 (t, 2 H, C(β)H_2, J = 6.7 Hz); 3.48 (s, 3 H, $CH_2OC\underline{H}_3$); 3.64 (s, 3 H, CO_2Me); 3.92 (s, 3 H, CO_2Me); 4.64 (s, 2 H, $C\underline{H}_2$OMe); 4.72 (br.s, 1 H, =CH—); 7.35 (d, 2 H, Ph, J = 8.7 Hz); 7.53 (d, 2 H, Ph, J = 8.7 Hz); 7.90 (s, 1 H, C(2)H). ^{13}C NMR, δ: 12.0, 26.6, 36.1, 47.6, 50.7, 52.9, 58.6, 66.7, 83.4, 122.8, 128.5 (2 C), 129.9 (2 C), 132.1, 135.4, 135.5, 136.1, 145.7, 153.7, 157.4, 163.5, 166.2, 168.3. MS (DART MS), m/z: 520.1234 [M + H]$^+$.

Dimethyl (2*E*)-2-(ethyl{2-[6-methoxymethyl-3-(2-methoxyphenyl)-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-5-yl]ethyl}amino)but-2-enedioate (19b). Yield 12%, white crystals, m.p. 147—149 °C, R_f 0.55 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 58.31; H, 5.72; N, 8.14. $C_{25}H_{29}N_3O_7S$. Calculated (%): C, 58.24; H, 5.67; N, 8.15. IR, ν/cm^{-1}: 1732, 1692, 1671 (C=O). ^{1}H NMR, δ: 1.09 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 6.8 Hz); 3.14—3.19 (m, 2 H, N—$C\underline{H}_2$Me); 3.23 (t, 2 H, C(α)H_2, J = 7.2 Hz); 3.35—3.39 (m, 2 H, C(β)H_2); 3.48 (s, 3 H, $CH_2OC\underline{H}_3$); 3.63 (s, 3 H, CO_2Me); 3.82 (s, 3 H, Ph—$OC\underline{H}_3$); 3.91 (s, 3 H, CO_2Me); 4.63 (s, 2 H, $C\underline{H}_2$OMe); 4.71 (br.s, 1 H, =CH—); 7.08—7.12 (m, 2 H, Ph); 7.31 (dd, 1 H, Ph, J = 8.2 Hz, J = 1.4 Hz); 7.49 (dt, 1 H, Ph, J = 8.2 Hz, J = 1.4 Hz); 7.90 (s, 1 H, C(2)H). ^{13}C NMR, δ: 15.2, 25.6, 36.1, 47.6, 50.7, 52.8, 55.8, 58.5, 66.7, 83.2, 112.4, 121.0, 123.0, 125.5, 129.1, 131.1, 132.2, 135.2, 147.2,

153.8, 154.6, 157.4, 163.5, 166.1, 168.3. MS (DART MS), *m/z*: 516.1796 $[M + H]^+$.

Methyl (2*E*)-3-(ethyl{2-[6-methoxymethyl-3-(2-methoxyphenyl)-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-5-yl]ethyl}amino)acrylate (19c). Yield 44%, white crystals, m.p. 126—128 °C, R_f 0.67 (Sorbfil, ethyl acetate—hexane, 1 : 1). Found (%): C, 60.42; H, 6.02; N, 9.17. $C_{23}H_{27}N_3O_5S$. Calculated (%): C, 60.38; H, 5.95; N, 9.18. IR, ν/cm^{-1}: 1679 (C=O). ^{1}H NMR, δ: 1.08 (t, 3 H, N—$CH_2C\underline{H}_3$, J = 6.9 Hz); 3.13 (q, 2 H, N—$C\underline{H}_2$Me, J = 6.9 Hz); 3.20 (t, 2 H, C(α)H_2, J = 6.3 Hz); 3.40 (t, 2 H, C(β)H_2, J = 6.3 Hz); 3.46 (s, 3 H, $CH_2OC\underline{H}_3$); 3.65 (s, 3 H, Ph—$OC\underline{H}_3$); 3.82 (s, 3 H, CO_2Me); 4.57—4.70 (m, 3 H, $C\underline{H}_2$OMe, CH=C$\underline{H}$—CO_2Me); 7.05—7.13 (m, 2 H, Ph); 7.33 (dd, 1 H, Ph, J = 7.8 Hz, J = 1.4 Hz); 7.41—7.49 (m, 2 H, Ph, C$\underline{H}$=CH—CO_2Me); 7.90 (s, 1 H, C(2)H). ^{13}C NMR, δ: 14.5, 24.5, 43.1, 50.4, 55.5, 55.8, 58.5, 66.8, 83.4, 112.3, 121.0, 123.1, 125.5, 129.1, 131.1, 132.9, 134.6, 147.3, 151.1, 154.6, 157.4, 163.5, 170.2. MS (DART MS), *m/z*: 458.1754 $[M + H]^+$.

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