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SYNTHESIS AND REACTIONS OF 1-R-3-BENZOYL-5-ETHOXY-CARBONYL-6-OXO-1,2,3,6-TETRA-HYDROPYRIDINE-2-THIONES

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Cycloacylation of N-R-3-oxo-3-phenylpropanethioamides by diethyl ethoxymethylenemalonate occurs selectively to form 1-R-3-benzoyl-5-ethoxycarbonyl-6-oxo-1,2,3,6-tetrahydropyridine-2-thiones which are convenient starting materials for the synthesis of bi- and tricyclic hetero systems including the previously unknown 9-R-7-ethoxycarbonyl-5-phenyl-8,9-dihydropyrido[2,3-d][1,2,4]triazolo[1,5-a]-pyrimidin-8-ones.

Keywords: 1-R-3-benzoyl-5-ethoxycarbonyl-6-oxo-1,2,3,6-tetrahydropyridine-2-thiones, diethyl ethoxymethylenemalonate, 6-ethoxycarbonyl-2-imino-8-methyl-4-phenyl-1,2,7,8-tetrahydropyrido[2,3-*d*]-pyrimidin-7-one, 5-ethoxycarbonyl-7-methy-3-phenyl-6,7-dihydroisoxazolo[3,4-*b*]pyridine-6-one, N-R-3-oxo-3-phenylpropanethioamides, 9-R-7-ethoxycarbonyl-5-phenyl-8,9-dihydropyrido[2,3-*d*][1,2,4]triazolo-[1,5-*a*]pyrimidin-8-ones, X-ray structural analysis, cycloacylation.

The cycloacylation of thioamides by unsaturated carboxylic acid derivatives is a convenient and practical method for the synthesis of sulfur containing azoles and azines [1-5].

One of these reagents is diethyl ethoxymethylenemalonate, the ethoxy group of which has good nucleofuge properties. None the less, there are only two studies in which the cyclocondensation of this compound with thioamides is discussed [6, 7]. It is likely that the low interest of investigators in this area of reactions is explained by the fact that the reaction is carried out under forcing conditions [7] and forms two [7] or three products [6].

The aim of this work was the discovery of conditions for the cycloacylation of the N-R-3-oxo-3-phenylpropanethioamides **1a,b** by diethyl ethoxymethylenemalonate **2** and the exploitation of the synthetic potential of the products obtained.

It was found that the N-R-3-oxo-3-phenylpropanethioamides **1a,b** condense with diethyl ethoxymethylenemalonate **2** in the presence of sodium ethylate. The reaction occurs selectively and its products are the 1-R-3-benzoyl-5-ethoxycarbonyl-6-oxo-1,2,3,6-tetrahydropyridine-2-thiones **3a,b**.

In all likelihood the high selectivity of the process is explained by the high CH-acidity of the thioamides **1a,b** [8] when compared with the N-aryl-2-thiocarbamoylacetamides. The latter react with diethyl ethoxymethylenemalonate non selectively to give three products [6].

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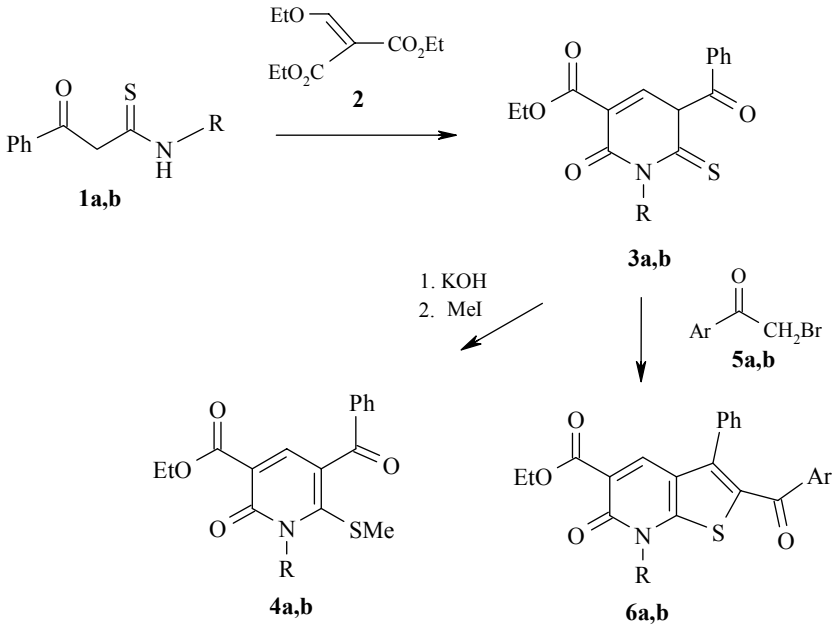
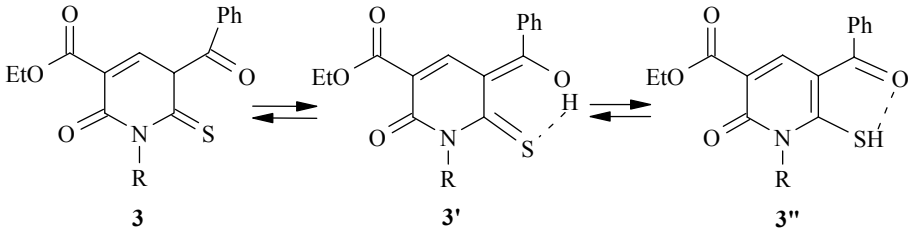


1, **3**, **4**, **6** **a** R = Me, **b** R = Et; **5**, **6** **a** Ar = Ph, **b** Ar = 4-ClC_6H_4

The yields of the compounds synthesized, melting points, and elemental analytical data are given in Table 1. The ^{1}H NMR and IR spectra are given in Table 2 and ^{13}C NMR spectra in Table 3. The structure of the products **3a,b** was proved by their reactions to the S-methyl derivatives **4a,b** and 2-aroyl-5-ethoxycarbonyl-3-phenyl-7-R-6,7-dihydrothieno[2,3-*b*]pyridine-6-ones **6a,b** (using methyl iodide and the arylbromomethyl ketones **5a,b** respectively).

Because the 1-R-1,2,3,6-tetrahydropyridine-2-thiones **3a,b** are structurally similar to β-thioxoketones [9] and can exist as an equilibrium mixture of the ketone **3**, enol **3'**, and enethiol **3"** forms as a result of the formation of intramolecular hydrogen bonds the spectra of compound **3b** were also recorded in $CDCl_3$ (^{1}H NMR) and CCl_4 (IR) to identify the structure of the dominant tautomer.



Analysis of the IR spectra showed that both in the solid state and in CCl_4 solution the 1-R-1,2,3,6-tetrahydropyridine-2-thiones **3a,b** occur in the enol form **3'** stabilized by a medium intensity hydrogen bond (ν_{OH} 3300 cm^{-1}) and the absorption for the mercapto group at 2500 cm^{-1} is absent. It did not prove possible to identify the ketonic form from the carbonyl group absorption bands because there are three carbonyl groups present in compounds **3a,b**, two of which do not take part in the formation of an intramolecular hydrogen bond.

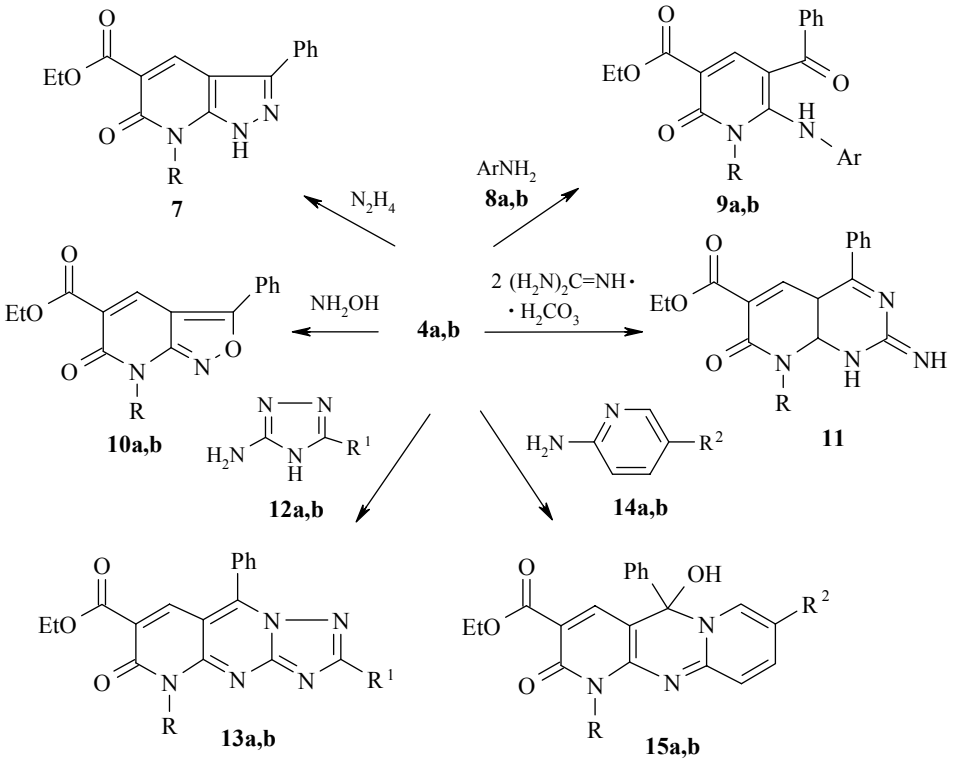
The ^{1}H NMR spectra of compound **3a,b** recorded in DMSO-d_6 do not show signals for the OH or SH group protons probably as a result of deuterium exchange whereas the ^{1}H NMR spectrum of the products **3a,b** show a proton signal at 14.14-14.60 ppm in $CDCl_3$ solution. Since the chemical shifts of chelated OH and SH

are at 12-18 and 4.5-7.5 ppm [10] the range of chemical shifts 14.14-14.60 ppm can most probably be assigned both to that of an enolic OH group signal and to the mean value of the enolic OH and enethiol SH form with a predominance of enol form **3'**.

The 1-R-3-benzoyl-5-ethoxycarbonyl-6-oxo-1,2,3,6-tetrahydropyridine-2-thiones **3a,b** and 1-R-5-benzoyl-3-ethoxycarbonyl-6-methylthio-1,2-dihydropyridin-2-ones **4a,b** are polyfunctional compounds and this makes them valuable starting materials for subsequent reactions. In contrast to 1,2,3,6-tetrahydropyridine-2-thiones **3a,b** we have found that the 1,2-dihydropyridine-2-ones **4a,b** readily take part in [3+2] and [3+3] cyclocondensations with nitrogen containing 1,2- and 1,3-dinucleophiles to give bi- and tricyclic heterocycles. It should be noted that these reactions occur selectively involving the methylthio- and phenylcarbonyl groups of the 1,2-dihydropyridine-2-ones **4a,b** and are accompanied by the evolution of methyl mercaptan and water. The product yields are preparative (60-78%).

We have used hydrazine and hydroxylamine as the 1,2-dinucleophiles. The 1,2-dihydropyridin-2-one **4a** reacts rapidly and unambiguously with hydrazine to give 5-ethoxycarbonyl-7-methyl-3-phenyl-6,7-dihydro-1H-pyazolo[3,4-b]pyridine-6-one **7**. It structure was confirmed using ^{1}H NMR and IR spectroscopy and composition from elemental analytical data.

Treatment of 1,2-dihydropyridin-2-ones **4a,b** with hydroxylamine can give the two products 6,7-dihydroisoxazolo[3,4-b]pyridine-6-ones and 6,7-dihydroisoxazolo[5,4-*b*]pyridine-6-ones. To clarify which of the reaction centers of the 1,2-dihydropyridin-2-ones **4a,b** (the methylthio or phenylcarbonyl group) primarily undergo nucleophilic attack we studied the reaction of the starting compound **4a** with aromatic amines. In the latter role we have used aniline and p-anisidine since their pK_a values (4.58 and 5.29 respectively) are close to that of hydroxylamine (5.97) [11]. As might be expected, methyl mercaptan is eliminated more readily than water to give the 6-arylamino-5-benzoyl-3-ethoxycarbonyl-1-methyl-1,2-dihydropyridine-2-ones **9a,b**.



8, **9 a** Ar = Ph, **b** Ar = 4-MeOC$_6$H$_4$; **7**, **9a**,**b**, **10a**, **11**, **13a**,**b**, **15a** R = Me;
10b, **15 b** R = Et; **12, 13 a** R^1 = H, **b** R^1 = SMe; **14**, **15 a** R^2 = H, **b** R^2 = Me

Since the reaction of the 1,2-dihydropyridine-2-ones **4a,b** with hydroxylamine occurs selectively it can be established on the basis of the above results that the products of this reaction are the 7-R-5-ethoxycarbonyl-3-phenyl-6,7-dihydroisoxazolo[3,4-*b*]pyridine-6-ones **10a,b**.

We have also studied the cyclocondensation of 1,2-dihydropyridin-2-ones **4a,b** with such nitrogen containing 1,3-dinucleophiles as guanidine carbonate, 5-R^1-3-amino-1,2,4-triazoles **12a,b**, and 5-R^2-2-aminopyridines **14a,b**.

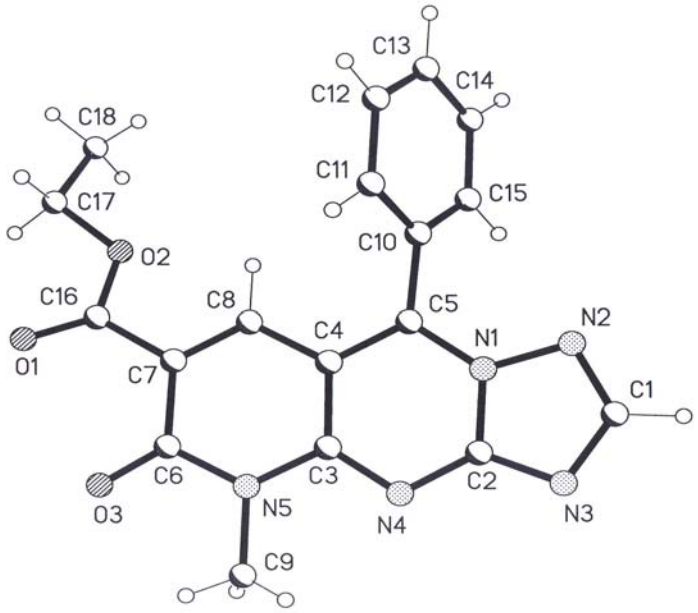


Fig. 1. Overall view of the 7-ethoxycarbonyl-9-methyl-5-phenyl-8,9-dihydropyrido[2,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-8-one molecule **13a**. Selected bond lengths and angles: $C_{(3)}$–$N_{(5)}$ 1.381(3), $C_{(3)}$–$C_{(4)}$ 1.425(3), $C_{(4)}$–$C_{(8)}$ 1.425(3), $C_{(4)}$–$C_{(5)}$ 1.377(3), $C_{(5)}$–$N_{(1)}$ 1.357(2), $N_{(1)}$–$C_{(2)}$ 1.386(3), $C_{(2)}$–$N_{(4)}$ 1.344(3), $N_{(4)}$–$C_{(3)}$ 1.323(2), $C_{(2)}$–$N_{(3)}$ 1.329(3), $N_{(3)}$–$C_{(1)}$ 1.350(3), $C_{(1)}$–$N_{(2)}$ 1.322(3), $N_{(2)}$–$N_{(1)}$ 1.373(2) Å; $N_{(5)}C_{(3)}N_{(4)}$ 117.42(18), $N_{(5)}C_{(3)}C_{(4)}$ 118.25(17), $C_{(8)}C_{(4)}C_{(3)}$ 118.79(17), $C_{(8)}C_{(4)}C_{(5)}$ 121.75(17), $C_{(4)}C_{(5)}N_{(1)}$ 115.34(17), $C_{(3)}N_{(4)}C_{(2)}$ 115.49(17), $N_{(4)}C_{(2)}N_{(1)}$ 122.34(18), $N_{(4)}C_{(2)}N_{(3)}$ 128.4(2), $N_{(1)}C_{(2)}N_{(3)}$ 109.3(2), $N_{(1)}N_{(2)}C_{(1)}$ 100.2(2), $N_{(2)}C_{(1)}N_{(3)}$ 118.4(2), $C_{(1)}N_{(3)}C_{(2)}$ 102.0(2)°.

It should be noted that the lower basicity 1,3-nucleophiles 2-aminopyrimidine and 5-aminotetrazole do not react with the dihydropyridin-2-ones **4a,b**.

The reaction of 1,2-dihydropyridin-2-one **4a** with guanidine gives only the 6-ethoxycarbonyl-2-imino-8-methyl-4-phenyl-1,2,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-7-one **11** in 70% yield whereas treatment of **4a,b** with 5-R^2-2-aminopyridines **14a,b** (5-R^1-3-amino-1,2,4-triazoles **12a,b**) can give two (four) isomeric heterocycles. However, these reactions occur selectively. The structure of the condensation products of **4a** with 5-R^1-3-amino-1,2,4-trazoles **12a,b** could not be determined by spectroscopic means hence their structures were studied using X-ray investigation. The X-ray data study for compound **13a** unambiguously shows that is 7-ethoxycarbonyl-9-methyl-5-phenyl-8,9-dihydropyrido[2,3-*d*][1,2,4]triazolo[1,5-a]pyrimidin-8-one.

The overall view of the compound **13a** molecule and the bond lengths and valence angles are given in Figure 1. The central tricyclic system $N_{1\text{-}5}C_{1\text{-}8}$ is virtually planar (the deviation from the mean square plane not exceeding 0.07 Å) and the dihedral angles between the heterocycle $C_{(4)}C_{(3)}N_{(4)}C_{(2)}N_{(1)}C_{(5)}$ and the systems

TABLE 1. Characteristics of the Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
3a	$C_{16}H_{15}NO_4S$	60.72 / 60.56	4.89 / 4.76	4.20 / 4.41	185-187	63
3b	$C_{17}H_{17}NO_4S$	61.85 / 61.62	4.88 / 5.17	3.94 / 4.23	135-137	68
4a	$C_{17}H_{17}NO_4S$	61.41 / 61.62	5.28 / 5.17	4.42 / 4.23	130-132	72
4b	$C_{18}H_{19}NO_4S$	62.42 / 62.59	5.73 / 5.54	3.85 / 4.06	98-100	76
6a	$C_{24}H_{19}NO_4S$	68.83 / 69.05	4.32 / 4.59	3.12 / 3.36	186-188	85
6b	$C_{25}H_{20}ClNO_4S$	64.55 / 64.44	4.60 / 4.33	2.88 / 3.01	170-173	81
7	$C_{16}H_{15}N_3O_3$	64.86 / 64.64	4.82 / 5.09	13.89 / 14.13	240-242	86
9a	$C_{22}H_{20}N_2O_4$	70.29 / 70.20	5.18 / 5.36	7.71 / 7.44	159-161	79
9b	$C_{23}H_{22}N_2O_5$	68.13 / 67.97	5.21 / 5.46	7.05 / 6.89	185-187	82
10a	$C_{16}H_{14}N_2O_4$	64.16 / 64.42	4.95 / 4.73	9.11 / 9.39	128-130	75
10b	$C_{17}H_{16}N_2O_4$	65.19 / 65.38	4.98 / 5.16	9.25 / 8.97	85-87	87
11	$C_{17}H_{16}N_4O_3$	63.12 / 62.96	5.22 / 4.97	17.52 / 17.27	176-178	70
13a	$C_{18}H_{15}N_5O_3$	62.05 / 61.89	4.48 / 4.33	19.82 / 20.05	228-230	66
13b	$C_{19}H_{17}N_5O_3S$	57.90 / 57.71	4.06 / 4.33	17.93 / 17.71	260-262	69
15a	$C_{21}H_{19}N_3O_4$	67.07 / 66.83	4.80 / 5.07	10.84 / 11.13	248-250	60
15b	$C_{22}H_{21}N_3O_4$	67.58 / 67.51	5.13 / 5.41	10.52 / 10.74	213-215	64

$C_{(4)}C_{(8)}C_{(7)}C_{(6)}N_{(5)}C_{(3)}$ and $N_{(1)}C_{(2)}N_{(3)}C_{(1)}N_{(2)}$ are 2.8 and 1.2º. The atoms $N_{(1)}$ and $N_{(5)}$ have planar trigonal coordination and the sum of the valence angles for these atoms is 360.0º. For steric reasons the benzene ring $C_{(10)}$-$C_{(15)}$ is twisted by 61.0º relative to the central fragment. It should be noted that, according to the Cambridge structural data bank [12], similar tricyclic systems have not been investigated by structural methods before.

In contrast to the reaction above, cyclocondensation of the 1,2-dihydropyridin-2-ones **4a,b** with the 5-R^2-2-aminopyridines **14a,b** cannot be accompanied by the separation of water and so its products can be compounds with both acyclic and cyclic structures. ^{1}H NMR and IR spectroscopic data were insufficient for an unambiguous identification of the reaction products hence their structure was determined using ^{13}C NMR spectroscopy.

It is known that the signal of a phenylcarbonyl group carbon atom occurs in the region 192.6-198.1 ppm in the ^{13}C NMR spectrum (Table 2, compounds **4b,9b** and the spectroscopic data in the study [13]). The ^{13}C NMR spectrum of compound **15a** does not show signals in the region but shows a signal for an sp^3-hybridized C–N carbon [14] with a chemical shift of 88.8 ppm. The latter can only be assigned to the $C_{(5)}$ atom of the 1-R-8-R^2-3-ethoxycarbonyl-5-hydroxy-5-phenyl-1,5-dihydro-2H-dipyrido[1,2-a:2,3-d]pyrimidin-2-ones **15a,b**.

Hence the cycloacylation of N-R-3-oxo-3-phenylpropanethioamides by diethyl ethoxymethylenemalonate occurs selectively and is a preparative method for obtaining 1-R-3-benzoyl-5-ethoxycarbonyl-6-oxo-1,2,3,6-tetrahydropyridine-2-thiones. These are valuable starting compounds for the preparation of bi- and tricyclic hetero systems including the previously unknown 9-R-7-ethoxycarbonyl-5-phenyl-8,9-dihydropyrido[2,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-8-ones.

TABLE 2. ^{1}H and ^{13}C NMR Spectroscopic Characteristics of the Compounds Synthesized

Com-pound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz)
1	2	3
3a	3300, 3000, 1660, 1620, 1550, 1450, 1390, 1380, 1350, 1310	1.27 (3H, t, *J* = 6.6, CH_3CH_2); 3.63 (3H, s, NCH_3); 4.25 (2H, q, *J* = 6.6, CH_3CH_2); 7.40 (2H, m, C_6H_5); 7.49 (1H, m, C_6H_5); 7.71 (2H, m, C_6H_5); 7.74 (1H, s, H-4) [1.41 (3H, t, *J* = 5.7, CH_3CH_2); 3.96 (3H, s, NCH_3); 4.44 (2H, q, *J* = 5.7, CH_3CH_2); 7.48-7.61 (3H, m, C_6H_5); 7.76 (1H, s, H-4); 7.90 (2H, m, C_6H_5); 14.60 (1H, br. s, OH)]*
3b*[2]	3300, 3050, 3000, 2900, 1670, 1620, 1550, 1430, 1390, 1360, 1270, 1210, 1180	1.19 (3H, t, *J* = 7.2, CH_3CH_2N); 1.28 (3H, t, *J* = 7.5, CH_3CH_2O); 4.26 (2H, q, *J* = 7.5, CH_3CH_2O); 4.38 (2H, q, *J* = 7.2, CH_3CH_2N); 7.43 (2H, m, C_6H_5); 7.56 (1H, m, C_6H_5); 7.70 (2H, m, C_6H_5); 7.73 (1H, s, H-4) [1.37 (6H, m, $2CH_3CH_2$); 4.39 (2H, q, *J* = 7.2, CH_3CH_2); 4.74 (2H, q, *J* = 6.9, CH_3CH_2); 7.46 (2H, m, C_6H_5); 7.56 (1H, m, C_6H_5); 7.74 (1H, s, H-4); 7.85 (2H, m, C_6H_5); 14.14 (1H, br. s, OH)]*
4a	3050, 3000, 1720, 1650, 1600, 1520, 1450, 1410, 1380, 1350, 1310	1.25 (3H, t, *J* = 6.9, CH_3CH_2); 2.32 (3H, s, SCH_3); 3.72 (3H, s, NCH_3); 4.21 (2H, q, *J* = 6.9, CH_3CH_2); 7.53 (2H, m, C_6H_5); 7.67 (1H, m, C_6H_5); 7.85 (2H, m, C_6H_5); 7.89 (1H, s, H-4)
4b	3000, 2950, 1690, 1670, 1650, 1580, 1490, 1460, 1380, 1350, 1310	1.29 (6H, m, $2CH_3CH_2$); 2.35 (3H, s, SCH_3); 4.19 (2H, q, *J* = 7.2, CH_3CH_2O); 4.36 (2H, q, *J* = 6.6, CH_3CH_2N); 7.55 (2H, m, C_6H_5); 7.68 (1H, m, C_6H_5); 7.84 (2H, m, C_6H_5); 7.87 (1H, s, H-4)
6a	3100, 3000, 1730, 1660, 1620, 1590, 1520, 1490, 1440, 1380, 1340, 1300, 1260, 1200	1.24 (3H, t, *J* = 7.2, CH_3CH_2); 3.70 (3H, s, NCH_3); 4.20 (2H, q, *J* = 7.2, CH_3CH_2); 7.16-7.25 (7H, m, C_6H_5); 7.32 (1H, m, C_6H_5); 7.43 (2H, m, C_6H_5); 8.00 (1H, s, H-4)
6b	3100, 3000, 2900, 1700, 1675, 1630, 1590, 1520, 1480, 1450, 1390, 1310	1.24 (3H, t, *J* = 7.2, CH_3CH_2N); 1.38 (3H, t, *J* = 6.9, CH_3CH_2O); 4.21 (4H, m, $2CH_3CH_2$); 7.14-7.28 (7H, m, H_{Ar}); 7.41 (2H, d, *J* = 8.9, 4-C_6H_4); 8.00 (1H, s, H-4)
7	3200, 3000, 1710, 1690, 1610, 1530, 1490, 1410, 1370, 1360	1.30 (3H, t, *J* = 7.2, CH_3CH_2); 3.53 (3H, s, NCH_3); 4.24 (2H, q, *J* = 7.2, CH_3CH_2); 7.55 (3H, m, C_6H_5); 7.82 (2H, m, C_6H_5); 8.46 (1H, s, H-4); 14.01 (1H, br. s, NH)
9a	3100, 3000, 1700, 1680, 1600, 1550, 1490, 1450, 1400, 1360	1.22 (3H, t, *J* = 6.6, CH_3CH_2); 3.26 (3H, s, NCH_3); 4.20 (2H, q, *J* = 6.6, CH_3CH_2); 6.96 (2H, m, C_6H_5); 7.08 (1H, s, C_6H_5); 7.23 (2H, m, C_6H_5); 7.45 (4H, m, C_6H_5); 7.54 (1H, m, C_6H_5); 8.20 (1H, s, H-4); 10.69 (1H, s, NH)
9b	3100, 3000, 1720, 1650, 1610, 1560, 1520, 1470, 1370, 1330	1.20 (3H, t, *J* = 7.2, CH_3CH_2); 3.18 (3H, s, NCH_3); 3.73 (3H, s, OCH_3); 4.13 (2H, q, *J* = 7.2, CH_3CH_2); 6.83 (2H, d, *J* = 8.1, 4-C_6H_4); 7.01 (2H, d, *J* = 8.1, 4-C_6H_4); 7.45-7.56 (5H, m, C_6H_5); 8.20 (1H, s, H-4); 11.04 (1H, s, NH)
10a	3100, 3000, 1700, 1670, 1630, 1540, 1480, 1450, 1400, 1370	1.31 (3H, t, *J* = 6.6, CH_3CH_2); 3.43 (3H, s, NCH_3); 4.30 (2H, q, *J* = 6.6, CH_3CH_2); 7.64 (3H, m, C_6H_5); 8.02 (2H, m, C_6H_5); 8.52 (1H, s, H-4)
10b	3100, 3000, 2950, 1730, 1640, 1540, 1480, 1460, 1390, 1340	1.32 (6H, m, $2CH_3CH_2$); 4.03 (2H, q, *J* = 6.9, CH_3CH_2N); 4.29 (2H, q, *J* = 6.9, CH_3CH_2O); 7.65 (3H, m, C_6H_5); 8.01 (2H, m, C_6H_5); 8.51 (1H, s, H-4)
11	3400, 3280, 3000, 1690, 1660, 1600, 1550, 1470, 1420, 1380	1.23 (3H, t, *J* = 7.3, CH_3CH_2); 3.56 (3H, s, NCH_3); 4.17 (2H, q, *J* = 7.3, CH_3CH_2); 6.92 (1H, s, NH); 7.59 (5H, m, C_6H_5); 7.71 (1H, s, HN=); 8.19 (1H, s, H-5)
13a	3100, 3000, 1730, 1660, 1630, 1600, 1550, 1530, 1490, 1450, 1380	1.24 (3H, t, *J* = 6.6, CH_3CH_2); 3.71 (3H, s, NCH_3); 4.25 (2H, q, *J* = 6.6, CH_3CH_2); 7.74 (5H, m, C_6H_5); 8.03 (1H, s, H-6); 8.61 (1H, s, H-2)

* Spectrum obtained in $CDCl_3$

*[2] IR spectrum of compound **3b** in CCl_4 (concentration 0.1 M): 3300, 3100, 3000, 2950, 1660, 1620, 1560, 1430, 1380, 1361, 1270, 1215.

TABLE 2. (continued)

1	2	3
13b	3100, 3000, 1740, 1670 1620, 1600, 1560, 1500, 1430, 1385, 1370, 1300	1.24 (3H, t, *J* = 7.2, C<u>H</u>$_3$CH$_2$); 2.58 (3H, s, SCH$_3$); 3.68 (3H, s, NCH$_3$); 4.23 (2H, q, *J* = 7.2, CH$_3$C<u>H</u>$_2$); 7.74 (5H, m, C$_6$H$_5$); 7.99 (1H, s, H-6)
15a	3100, 3000, 1720, 1640, 1620, 1580, 1560, 1480, 1370, 1300	1.15 (3H, t, *J* = 6.9, C<u>H</u>$_3$CH$_2$); 3.54 (3H, s, NCH$_3$); 4.09 (2H, q, *J* = 6.9, CH$_3$C<u>H</u>$_2$); 6.74 (1H, m, H-8); 7.08 (1H, d, *J* = 9.0, H-10); 7.31-7.47 (5H, m, C$_6$H$_5$); 7.58 (1H, s, OH); 7.62 (1H, m, H-9); 7.71 (1H, d, *J* = 6. 6, H-7); 8.59 (1H, s, H-4)
15b	3100, 3000, 1720, 1640, 1610, 1580, 1490, 1460, 1370, 1340	1.19 (6H, m, 2C<u>H</u>$_3$CH$_2$); 2.05 (8-CH$_3$); 4.08 (2H, q, *J* = 6.9, CH$_3$C<u>H</u>$_2$O); 4.29 (2H, q, *J* = 7.2, CH$_3$C<u>H</u>$_2$ N); 7.00 (1H, d, *J* = 9.6, H-9); 7.33 (2H, m, Ar); 7.38-7.44 (3H, m, Ar); 7.49 (2H, m, Ar); 7.57 (1H, s, OH); 8.46 (1H, s, H-4)

TABLE 3. ^{13}C NMR Spectra of Compounds **4b**, **9b**, and **15a**

Com-pound	Chemical shifts (DMSO-d$_6$), δ, ppm.
4b	13.6 (NCH$_2$<u>C</u>H$_3$), 14.0 (OCH$_2$<u>C</u>H$_3$); 20.2 (SCH$_3$); 41.8 (N<u>C</u>H$_2$CH$_3$), 60.6 (O<u>C</u>H$_2$CH$_3$); 118.6, 121.7, 128.7, 129.6, 133.6, 138.8, 141.1, 151.6 (Ar); 157.9 (O=<u>C</u>–N); 163.9 (O=<u>C</u>–OEt); 192.6 (C$_6$H$_5$–<u>C</u>=O)
9b	14.2 (OCH$_2$<u>C</u>H$_3$); 33.1 (NCH$_3$); 55.3 (OCH$_3$); 59.7 (O<u>C</u>H$_2$CH$_3$); 102.4, 105.7, 114.4, 124.4, 128.3, 128.4, 131.6, 132.0, 138.2, 147.6, 156.0, 156.8 (Ar); 158.8 (O=<u>C</u>–N); 164.2 (O=<u>C</u>–OEt); 193.0 (C$_6$H$_5$–<u>C</u>=O)
15a	14.18 (OCH$_2$<u>C</u>H$_3$); 28.2 (NCH$_3$); 59.2 (O<u>C</u>H$_2$CH$_3$); 88.8 (C-5); 100.4, 107.8, 113.5, 123.3, 125.7, 128.5, 128.6, 135.6, 139.3, 141.9, 145.4, 149.9, 151.3 (Ar); 158.8 (O=<u>C</u>–N); 164.7 (O=<u>C</u>–OEt)

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Varian 300 instrument (300 and 75 MHz respectively) using TMS as internal standard. IR spectra were taken on a UR-20 instrument for KBr tablets.

X-ray Structural Investigation of Compound 13a Single Crystal with a linear size of 0.38×0.25×0.20 mm was prepared by a method of slow cooling of an ethanol solution and measured at room temperature on a Bruker Apex II automatic CCD diffractometer (MoK$_\alpha$ radiation, λ = 0.71069 Å, θ_{max} = 26.62º, spherical segment -9 ≤ h ≤ 12, -18 ≤ k ≤ 21, -24 ≤ l ≤ 15). In all, 11,993 reflections were collected (3247 independent reflections, R_{int} = 0.0305). Crystals of compound **13a** are orthorhombic with a = 10.1548(7), b = 16.9036(11), c = 19.354(2) Å, V = 3322.2(5) Å^3, M = 349.35, Z = 8, d_{calc} = 1.397 g/cm^3, μ = 0.099 cm^{-1}, F(000) = 1456, space group *Pbca* (No. 61). The structure was solved by a direct method and refined in a least squares analysis full matrix anisotropic approximation using the SHELXS97 [15] and SHELXL97 [16] programs. 3247 reflections were used in the refinement (2115 reflections with $I > 2\sigma(I)$) (295 refinement parameters, number of reflections per parameter 7.17). All of the hydrogen atoms were revealed in electron density difference synthesis and included in the refinement with fixed positions and thermal parameters. A weighting scheme was used with $w = 1/[s^2(F_0^2) + (0.0754P)^2 + 0.5696P]$, where $P = (F_0^2 + 2F_c^2)/3$. The final difference factors were $R_1(F)$ = 0.0481 and $wR_2(F^2)$ = 0.1207 and GOF = 1.002. The residual electron density from the Fourier difference series was -0.272 and 0.215 e/Å^3. The full set of structural data for compound **13a** has been deposited in the Cambridge structural data bank (CCDC 653195).

1-R-3-Benzoyl-5-ethoxycarbonyl-6-oxo-1,2,3,6-tetrahydropyridine-2-thiones 3a,b. A solution of sodium ethylate (0.1 mol), the thioamide **1a,b** (0.1 mol), and diethyl ethoxymethylenemalonate **2** (21.6 g, 0.1 mol) in anhydrous ethanol (100 ml) was refluxed with a reflux condenser for 2 h and then cooled. Hydrochloric acid (6%, 100 ml) was added and the precipitate was filtered off, dried, and recrystallized from ethanol (**3a**) or 2-propanol (**3b**).

1-R-5-Benzoyl-3-ethoxycarbonyl-6-methylthio-1,2-dihydropyridin-2-ones 4a,b. A solution of KOH (1.12 g, 0.02 mol), the tetrahydropyridine-2-thione **3a,b** (0.02 mol), and methyl iodide (3.408 g, 0.024 mol) in ethanol (90%, 50ml) was refluxed with a reflux condenser for 1 h and then cooled. Water (80 ml) was added and the precipitated **4a,b** were filtered off, dried, and recrystallized from 2-propanol.

7-R-2-Aroyl-5-ethoxycarbonyl-3-phenyl-6,7-dihydrothieno[2,3-*b*]pyridine-6-ones 6a,b. A solution of KOH (0.56 g, 0.01 mol), the tetrahydropyridine-2-thione **3a,b** (0.1 mol), and the arylbromomethyl ketone **5a,b** (0.01 mol) in ethanol (85%, 15 ml) was refluxed for 1 h, cooled and water (30 ml) was added. The precipitated **6a,b** were filtered off, dried, and crystallized from AcOH.

5-Ethoxycarbonyl-7-methyl-3-phenyl-6,7-dihydro-1H-pyrazolo[3,4-b]pyridin-6-one 7. A solution of the 1,2-dihydropyridin-2-one **4a** (1.655 g, 0.005 mol) and hydrazine monohydrate (0.25 g, 0.005 mol) in 2-propanol (8 ml) was refluxed with a reflux condenser for 30 min and cooled. The precipitated product **7** was filtered off, dried, and recrystallized from DMSO.

6-Arylamino-5-benzoyl-3-ethoxycarbonyl-1-methyl-1,2-dihydropyridin-2-ones 9a,b. A mixture of the 1,2-dihydropyridin-2-one **4a** (1.655 g, 0.005 mol) and arylamine **8a,b** (0.005 mol) was fused at 140ºC for 20 min and then cooled. The product **9a,b** was recrystallized from ethanol.

5-Ethoxycarbonyl-7-methyl-3-phenyl-6,7-dihydroisoxazolo[3,4-b]pyridin-6-ones 10a,b. A solution of hydroxylamine hydrochloride (0.348 g, 0.005 mol), KOH (0.28 g, 0.005 mol), 1,2-dihydropyridin-2-one **4a,b** (0.005 mol) and ethanol (5 ml) was refluxed with a reflux condenser for 1 h. The solution was separated from the KCl precipitate, cooled, and the product **10a,b** filtered.

6-Ethoxycarbonyl-2-imino-8-methyl-4-phenyl-1,2,7,8-tetrahydropyrido[2,3-d]pyrimidin-7-one (11). A mixture of the 1,2-dihydropyridin-2-one **4a** (1.655 g, 0.005 mol) and guanidine carbonate (0.54 g, 0.003 mol) was fused at 140ºC for 30 min, cooled, the reaction mixture dissolved in 2-propanol (6 ml), filtered from the unreacted guanidine carbonate, and cooled. The precipitate of **11** was separated and recrystallized from 2-propanol.

2-R^1-7-Ethoxycarbonyl-9-methyl-5-phenyl-8,9-dihydropyrido[2,3-*d*][1,2,4]triazolo[1.5-*a*]pyrimidin-8-ones (13a,b). A solution of the 1,2-dihydropyridin-2-one **4a** (1.655 g, 0.005 mol) and 5-R-3-amino-1,2,4-triazole **12a,b** (0.005 mol) in 2-propanol (6 ml) was refluxed for 1 h and then cooled. The product **13a,b** was filtered off, dried, and recrystallized from ethanol (**13a**) or DMSO (**13b**).

1-R-8-R^2-3-Ethoxycarbonyl-5-hydroxy-5-phenyl-1,5-dihydro[1,2-a:2,3-d]pyrimidin-2-ones (15a,b). A solution of the 1,2-dihydropyridin-2-one **4a,b** (0.005 mol) and 2-amino-5-R^2-pyridine **14a,b** (0.005 mol) in 2-propanol (5 ml) was refluxed with a reflux condenser for 1 h and then cooled. The product **15a,b** was filtered off, dried, and recrystallized from DMSO.

REFERENCES

1. N. A. Danilkina, L. E. Mikhailov, and B. A. Ivin, *Zh. Org. Khim.*, **42**, 807 (2006).
2. A. N. Borisevich, V. N. Britsun, and M. O. Lozinskii, *Zh. Org. Farm. Khim.*, **4**, 3 (2006).
3. V. N. Britsun, A. N. Borisevich, L. S. Samoilenko, and M. O. Lozinskii, *Zh. Org. Khim.*, **41**, 292 (2005).
4. V. N. Britsun, A. N. Borisevich, A. N. Esipenko, and M. O. Lozinskii, *Khim. Geterotsikl. Soedin.*, 623 (2006). [*Chem. Heterocycl. Comp.*, **42**, 546 (2006)].

5. A. D. Dyachenko, S. M. Desenko, V. D. Dyachenko, and A. N. Chernega, *Khim. Geterotsikl. Soedin.*, 1171 (2004). [*Chem. Heterocycl. Comp.*, **40**, 1009 (2004).
6. R. P. Tkachev, O. S. Bityukova, V. D. Dyachenko, V. P. Tkacheva, and A. D. Dyachenko, *Zh. Obshch. Khim.*, **77**, 125 (2007).
7. J. P. Clayton, P. J. O'Hanlon, and T. J. King, *J. Chem. Soc., Perkin Trans. 1*, 1352 (1980).
8. V. N. Britsun, V. O. Doroshuk, N. V. Bogdan, V. M. Zaitsev, and M. O. Lozinskii, *Ukr. Khim. Zh.*, **73**, No. 5, 40 (2007).
9. F. Duus, *J. Amer. Chem. Soc.*, **108**, 630 (1986).
10. U. Berg, J. Sandstrom, L. Carlsen, and F. Duus, *J. Chem. Soc., Perkin Trans. 2*, 1321 (1983).
11. A. Albert and E. P. Sergeant, *Ionization Constants of Acids and Bases*, [Russian translation], Khimiya, Moscow, Leningrad (1964), p. 139.
12. Cambridge Crystallographic Data Base, release 2007.
13. V. N. Britsun, A. N. Borisevich, L. S. Samoilenko, A. N. Chernega, and M. O. Lozinskii, *Izv. Akad. Nauk, Ser. Khim.*, 757 (2005).
14. E. Breitmaier and W. Voelter, *^{13}C NMR Spectroscopy*, 2nd Edition, Verlag Chemie, Weinheim (1978), p. 183.
15. G. M. Sheldrick, *SHELXS97. A Program for the Solution of Crystal Structures,* Göttingen University, Germany (1997).
16. G. M. Sheldrick, *SHELXL97. A Program for the Refinement of Crystal Structures*, Göttingen University, Germany (1997).