Fused sulfur-containing pyridine systems
1. Synthesis and structures of tetrahydropyridothienopyridinone and tetrahydropyridothiopyranopyridinone derivatives*

V. V. Dotsenko,[a]★ S. G. Krivokolysko,[a] A. N. Chernega,[b] and V. P. Litvinov[c]

[a]*East Ukrainian National University,*
20a-7 kv. Molodezhnyi, 91034 Lugansk, Ukraine.
Fax: (064 2) 41 9151. E-mail: ksg@lep.lg.ua
[b]*Institute of Organic Chemistry, National Academy of Sciences of Ukraine,*
5 ul. Murmanskaya, 02094 Kiev, Ukraine.
Fax: (044) 573 2643. E-mail: iochkiev@ukrpack.net
[c]*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,*
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (095) 135 5328. E-mail: vpl@cacr.ioc.ac.ru

The reactions of *N*-methylmorpholinium 4-aryl(hetaryl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates with malononitrile and acetone in ethanol afforded substituted tetrahydropyridothienopyridinones. In the absence of acetone, tetrahydropyridothiopyranopyridinones were isolated as the major reaction products. The latter were also synthesized independently by the reactions of the above-mentioned thiolates with 2-amino-1,1,3-tricyanopropene. The structure of 2,4-diamino-10-(2-chlorophenyl)-3-cyano-5-imino-8-oxo-7,8,9,10-tetrahydro-5*H*-pyrido[2′,3′:2,3]thiopyrano[4,5-b]pyridine was established by X-ray diffraction analysis.

Key words: tetrahydropyridinethiolates, malononitrile, acetone, 2-amino-1,1,3-tricyanopropene, multicomponent condensation, tetrahydropyridothienopyridinones, tetrahydropyridothiopyranopyridinones, X-ray diffraction analysis.

Partially hydrogenated pyridinethiones and the corresponding thiolates belong to a class of promising organic compounds, whose derivatives often exhibit high biological activity.[1—4] Of the reactions of these compounds, oxidation, halogenation, and alkylation with haloalkanes and their derivatives, which is sometimes followed by transformations into fused systems, have received most study.[1,3—8] However, procedures for the synthesis of polycyclic sulfur-containing pyridine derivatives based on pyridinethiones remain poorly developed. Earlier, we have been demonstrated[9] that the reactions of derivatives of ammonium tetrahydropyridinethiolates with malononitrile and acetone proceeded through cascade heterocyclization to form hydrogenated pyridothienopyridines, which is the second example of the directed synthesis of the above-mentioned type of compounds.[10]

The aim of the present study was to perform the reactions of *N*-methylmorpholinium 4-aryl(hetaryl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridinethiolates with malononitrile and acetone, examine the possibility of optimization of the reaction conditions using the multicomponent synthesis, and establish the structures of the reaction products.

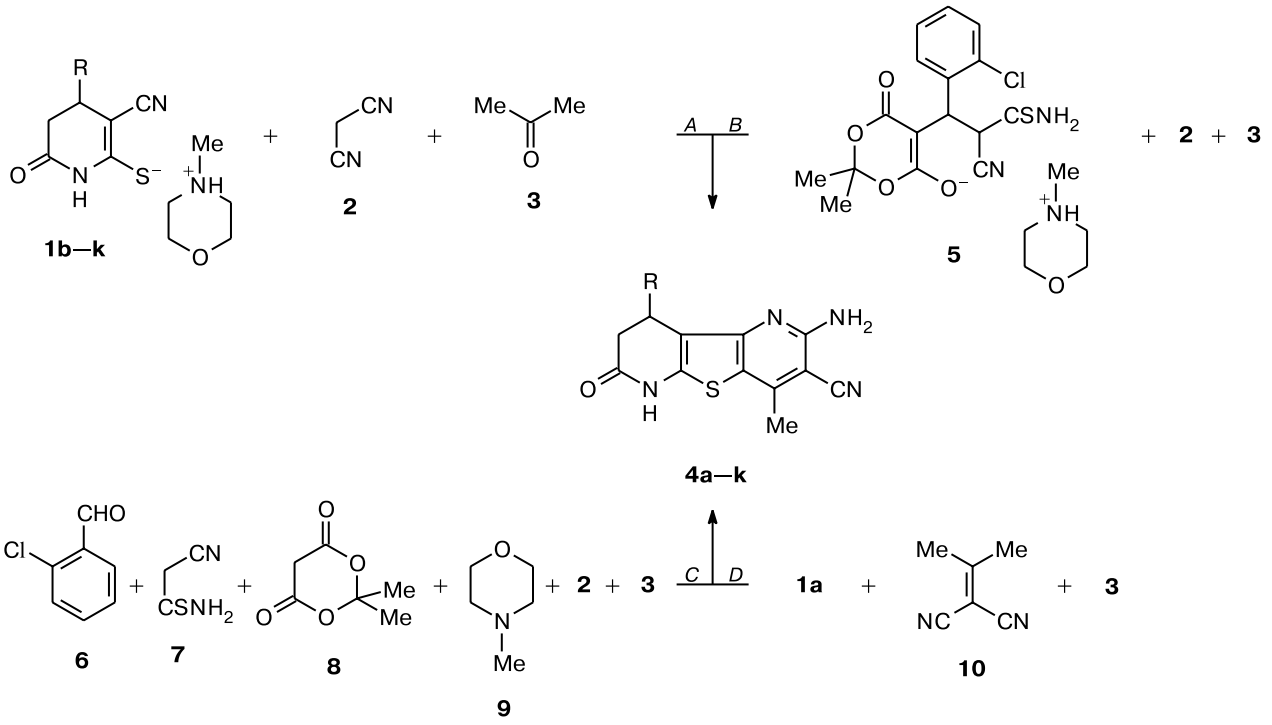
We have found that the reaction of tetrahydropyridine-6-thiolates **1**, malononitrile (**2**), and acetone (**3**) in refluxing EtOH serves as a general approach to the synthesis of pyridothienopyridinones **4** (method *A*) (Scheme 1). The same compounds were produced in the reactions of precursors of thiolates **1**, *viz.*, the corresponding Michael adducts,[4,11,12] with compounds **2** and **3** (method *B*), as exemplified by the transformation of known 1,3-dioxa-4-cyclohexenolate **5**.[12] A promising approach to the synthesis of compounds **4** is based on the *in situ* generation of Michael adduct **5** from 2-chlorobenzaldehyde (**6**), cyanothioacetamide (**7**), and Meldrum´s acid (**8**) in the presence of *N*-methylmorpholine (**9**) followed by the reactions of adduct **5** (without isolation and purification) with compounds **2** and **3** (method *C*). However, the method *A* proved to be the procedure of choice, because it afforded the target product in higher yield. For example, compound **4a** [9] was prepared in 37% yield according to the method *A*, whereas the methods *B* and *C* afforded **4a** in only 18.5% and 7% yields, respectively. It should be noted that the reaction times in the last two cases were much

* Dedicated to the blessed memory of Professor Yu. A. Sharanin.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 918—925, April, 2003.

1066-5285/03/5204-969 $25.00

Scheme 1



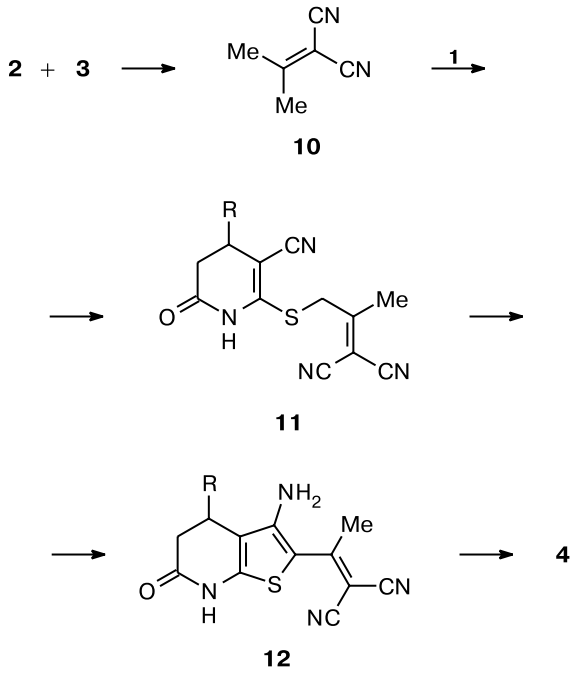
1, 4	**a**	**b**	**c**	**d**	**e**	**f**
R	2-ClC_6H_4	1-naphthyl	4-$EtOC_6H_4$	3,4-$(MeO)_2C_6H_3$	2,5-$(MeO)_2C_6H_3$	4-MeC_6H_4
1, 4	**g**	**h**	**i**	**j**	**k**	
R	3,4,5-$(MeO)_3C_6H_2$	2-thienyl	2-$MeOC_6H_4$	3,4-$(OCH_2O)C_6H_3$	Ph	

longer. The same product can be prepared in 33% yield by refluxing a mixture of thiolate **1a**, isopropylidenemalononitrile (1.5 equiv.) (**10**), and an excess of acetone in EtOH (method *D*). It was found that refluxing of a mixture of thiolate **1a** and nitrile **10** in EtOH for 12 h did not afford the expected thienodipyridine **4a**, whereas this compound was isolated after the addition of acetone followed by heating for 6—7 h. Apparently, nitrile **10** is involved in the retro-Knoevenagel reaction on refluxing in 96% EtOH in the presence of bases. In this case, excess acetone can hinder the latter reaction. Evidently, the method *D* has no obvious advantages over the method *A*. A decrease in the yield of the target products in the reactions involving a larger number of components is, presumably, associated with the fact that side processes become more probable.

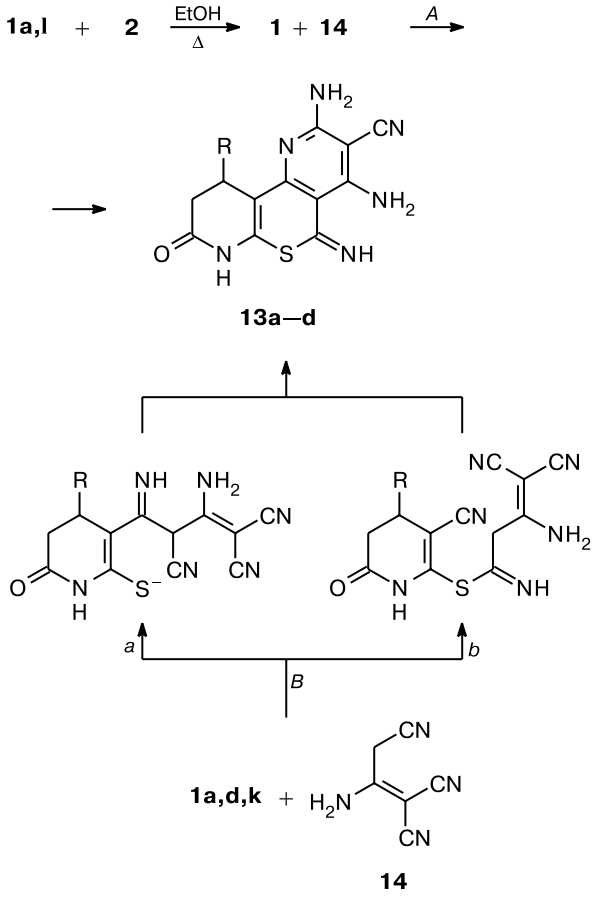
We hypothesize that the first step of the process involves Knoevenagel condensation of nitrile **2** with acetone giving rise to isopropylidenemalononitrile (**10**) (Scheme 2), which is confirmed by the fact that the synthesis can be carried out according to the method *D*. Compound **10** subsequently reacts with salt **1** to form dicyanoallyl derivative of pyridine (**11**). The formation of the C—S bond is the key factor in this step. This mode of formation of this bond in the synthesis of sulfides has not been reported earlier. The closest analog of the above-described reaction seems to be the mechanism of formation of thiols through *S*-functionalization of the Me group by thiolation with elemental sulfur in the presence of bases.[13] In particularly, this approach was used in the syntheses of substituted thiophenes from derivatives of methylene-active nitriles and sulfur by the modified Gewald reaction.[13,14] Apparently, pyridinethiolate **1** serves as a synthetic analog of activated sulfur in the above-mentioned thiolation. However, alternative mechanisms of formation of the C—S bond must not be ruled out. Atmospheric oxygen can act as an oxidizer necessary for this reaction. Although the data published in the literature and our experimental results do not allow us to unambiguously postulate the mechanism of formation of intermediate **11**, the generation of the latter is highly probable. Under the reaction conditions, cascade heterocyclization results in the Thorpe—Ziegler transformation of dicyanovinyl derivative **11** into thienopyridine **12**, which, in turn, is transformed into the final compound **4** as a result of the closure of the second pyridine ring. The latter two steps have a direct analogy in the literature,[10] which is evidence in favor of the proposed pathway of the reaction under study.

The assumed scheme of the formation of compounds **4** is also supported by the fact that the reaction took another

Scheme 2



Scheme 3



1l: R = 4-$MeOC_6H_4$,
13: R = 2-ClC_6H_4 (**a**), 4-$MeOC_6H_4$ (**b**), Ph (**c**), 3,4-$(MeO)_2C_6H_3$ (**d**)

pathway in the absence of acetone. Refluxing of tetrahydropyridinethiolates **1** in EtOH with a threefold excess of nitrile **2** afforded pyridothiopyranopyridones **13** as the major reaction products (Scheme 3, method *A*). Based on the structures of the reaction products, we hypothesizes that the initial step of the reaction involves dimerization of nitrile **2** in a basic medium giving rise to 2-amino-1,1,3-tricyanopropene (**14**). It was found that thiolates **1** did react with the dimer of malononitrile **14** on refluxing in EtOH to give the same products **13** in even higher yields (method *B*). In the latter case, the presence of even a tenfold excess of acetone with respect to thiolate **1** did not influence the direction of the reaction. The reactions of dimer **14** with salts **1** can take two pathways. One of them involves the attack of the 2-amino-1,1,3-tricyanopropene anion on the CN group of thiolate **1** to form the C—C bond followed by the closure of the thiopyran and pyridine rings (path *a*). Another pathway involves the nucleophilic attack of the thiolate ion on the nonconjugated nitrile group of tricyanopropene **14** to form the C—S bond followed by the successive closure of the thiopyran and pyridine rings (path *b*). We plan to investigate the mechanism of this reaction in the future.

The ^{1}H NMR spectra of pyridothienopyridinones **4** have two doublets of doublets at δ 2.66—3.32 belonging to $C(8)H_2$ and a doublet of doublets at δ 4.41—5.34 assigned to C(9)H, which are characteristic of the —CH(R)—CH_2— fragment of the tetrahydropyridine ring.[15,16] A broadened singlet of the amino group, a singlet of the NH group, and a signal of the C(4)Me group are observed at δ 6.04—6.35, 10.91—11.13, and 2.43—2.54, respectively (Table 1).

The ^{1}H NMR spectra of pyridothiopyranopyridinones **13** have analogous signals, *viz.*, two doublets of doublets for the protons of the $C(9)H_2$ group at δ 2.48—2.92 and a doublet of doublets for the protons of C(10)H at δ 4.92—5.29. The signal for the protons of the $C(2)NH_2$ group is observed as a broadened singlet at δ 5.98—6.44. The spectra of compounds **13** show three low-field singlets (the intensity of each singlet corresponds to 1 H). We believe that the signal at δ 9.60—9.76 corresponds to the imino group of the thiopyran ring (C(5)NH). By analogy with pyridothienopyridines **4**, the singlet at δ 10.34—10.52 should be assigned to the endocyclic imino group of the tetrahydropyridine ring. Presumably, the strongly broadened singlet (δ 10.85) and the analogous peak at δ 6.72—6.90 correspond to the $C(4)NH_2$ group. The splitting of the signal into two broadened singlets and a substantial downfield shift of one of these singlets can be attributed to the $C(4)NH_2$...C(5)NH hydrogen bond,

Table 1. Spectroscopic characteristics of compounds **4b—k** and **13a—d**

Compound	IR, ν/cm^{-1}	^1H NMR, δ (J/Hz)
4b	3480—3165 (NH, NH_2); 2196 (CN); 1680 (C=O)	2.54 (s, 3 H, C(4)Me); 2.72 (br.pseudod, 1 H, C(8)H, ^2J = 16.0)*; 3.32 (m, 1 H, C(8)H); 5.34 (br.pseudod, 1 H, C(9)H)*; 6.35 (br.s, 2 H, NH_2); 6.73—8.31 (m, 7 H, Ar); 11.13 (br.s, 1 H, NH)
4c	3550—3180 (NH, NH_2); 2197, 2183 sh (CN); 1680 (C=O)	1.32 (t, 3 H, $C\underline{H}_3CH_2$, ^3J = 6.9); 2.49 (s, 3 H, C(4)Me); 2.67 and 2.99 (both br.pseudod, 1 H each, C(8)H_2, ^2J = 16.2)*; 3.91 (q, 2 H, $CH_3C\underline{H}_2$, ^3J = 6.9); 4.46 (br.pseudod, 1 H, C(9)H)*; 6.18 (br.s, 2 H, NH_2); 6.70 and 7.02 (both d, 2 H each, Ar, ^3J = 8.3); 10.97 (br.s, 1 H, NH)
4d	3540, 3430, 3315, 3250—3150 (NH, NH_2); 2198 (CN); 1692 (C=O)	2.51 (s, 3 H, C(4)Me); 2.76 and 3.02 (both br.pseudod, 1 H each, C(8)H_2, ^2J = 16.6)*; 3.70 and 3.74 (both s, 3 H each, $(MeO)_2$); 4.48 (br.pseudod, 1 H, C(9)H)*; 6.19 (br.s, 2 H, NH_2); 6.55 and 6.70 (both d, 1 H each, Ar, ^3J = 8.2); 7.02 (s, 1 H, Ar); 10.99 (br.s, 1 H, NH)
4e	3465, 3345—3330, 3200 (NH, NH_2); 2207, 2193 sh (CN); 1675 (C=O)	2.53 (s, 3 H, C(4)Me); 2.66 (br.pseudod, 1 H, C(8)H, ^2J = 16.6)*; 2.93 (dd, 1 H, C(8)H, ^2J = 16.6, ^3J = 7.8); 3.59 and 3.86 (both s, 3 H each, $(MeO)_2$); 4.68 (br.pseudod, 1 H, C(9)H)*; 6.04 (br.s, 2 H, NH_2); 6.12 (s, 1 H, Ar); 6.64 and 6.82 (both d, 1 H each, Ar, ^3J = 8.6); 10.93 (br.s, 1 H, NH)
4f	3465, 3280, 3200 (NH, NH_2); 2201 (CN); 1689 (C=O)	2.19 (s, 3 H, Me_{Ar}); 2.43 (s, 3 H, C(4)Me); 2.68 and 3.00 (both br.pseudod, 1 H each, C(8)H_2, ^2J = 16.0)*; 4.41 (br.pseudod, 1 H, C(9)H)*; 6.06 (br.s, 2 H, NH_2); 6.96 (br.s, 4 H, Ar); 10.91 (br.s, 1 H, NH)
4g	3465, 3350—3180 (NH, NH_2); 2207, 2200 sh (CN); 1690 (C=O)	2.47 (s, 3 H, C(4)Me); 2.78 and 3.02 (both br.pseudod, 1 H each, C(8)H_2, ^2J = 16.3)*; 3.59 (s, 3 H, MeO); 3.69 (s, 6 H, $(MeO)_2$); 4.45 (br.pseudod, 1 H, C(9)H)*; 6.28 (br.s, 2 H, NH_2); 6.56 (s, 2 H, Ar); 11.01 (br.s, 1 H, NH)
4h	3600—3150 (NH, NH_2, OH); 2197 (CN); 1700, 1680 (2 C=O)	1.89 (s, 3 H, $C\underline{H}_3COOH$); 2.48 (s, 3 H, C(4)Me); 2.80 (br.pseudod, 1 H, C(8)H, ^2J = 16.3)*; 3.08 (dd, 1 H, C(8)H, ^2J = 16.3, ^3J = 7.1); 4.70 (br.pseudod, 1 H, C(9)H)*; 6.24 (br.s, 2 H, NH_2); 6.72 (m, 1 H, thienyl); 6.82 (m, 1 H, thienyl); 7.12 (m, 1 H, thienyl); 11.03 (br.s, 1 H, NH)**
4i	3460, 3350—3150 (NH, NH_2); 2197 (CN); 1670 (C=O)	2.52 (s, 3 H, C(4)Me); 2.67 (br.pseudod, 1 H, C(8)H, ^2J = 16.6)*; 3.02 (dd, 1 H, C(8)H, ^2J = 16.6, ^3J = 8.0); 3.91 (s, 3 H, MeO); 4.72 (br.pseudod, 1 H, C(9)H)*; 6.23 (br.s, 2 H, NH_2); 6.54 (d, ^3J = 7.5), 6.72 (m), 6.96 (d, ^3J = 8.1), 7.18 (m, 4 H, Ar); 10.97 (br.s, 1 H, NH)
4j	3465, 3320—3145 (NH, NH_2); 2200, 2185 sh (CN); 1690 (C=O)	2.50 (s, 3 H, C(4)Me); 2.67 and 2.98 (both br.pseudod, 1 H each, C(8)H_2, ^2J = 16.2)*; 4.44 (br.pseudod, 1 H, C(9)H)*; 5.10 (br.s, 2 H, OCH_2O); 6.25 (br.s, 2 H, NH_2); 6.53—6.73 (m, 3 H, Ar); 11.01 (br.s, 1 H, NH)
4k	3420, 3340, 3240 (NH, NH_2); 2204 (CN); 1675 (C=O)	2.49 (s, 3 H, C(4)Me); 2.70 (br.pseudod, 1 H, C(8)H, ^2J = 16.2)*; 3.08 (m, 1 H, C(8)H); 4.52 (br.pseudod, 1 H, C(9)H)*, 6.28 (br.s, 2 H, NH_2); 7.12—7.26 (m, 5 H, Ph); 11.01 (br.s, 1 H, NH)
13a	3570—3165 (2 NH, 2 NH_2); 2200, 2190 sh (CN); 1685 (C=O)	2.54 (br.pseudod, 1 H, C(9)H, ^2J = 16.1)*; 2.90 (dd, 1 H, C(9)H, ^2J = 16.1, ^3J = 8.0)*; 5.29 (br.pseudod, 1 H, C(10)H)*; 5.98 (br.s, 2 H, $C(2)NH_2$); 6.87 (br.s, 1 H, $C(4)NH_2$); 6.98—7.37 (m, 4 H, Ar); 9.76 (br.s, 1 H, C(5)NH); 10.52 (s, 1 H, NH); 10.85 (br.s, 1 H, $C(4)NH_2$)
13b	3500, 3435, 3340, 3235 (2 NH, 2 NH_2); 2194, 2179 sh (CN); 1684 (C=O)	2.57 (br.pseudod, 1 H, C(9)H, ^2J = 17.3)*; 2.88 (dd, 1 H, C(9)H, ^2J = 17.3, ^3J = 7.1); 3.70 (s, 3 H, MeO); 4.95 (br.pseudod, 1 H, C(10)H)*; 6.31 (br.s, 2 H, $C(2)NH_2$); 6.73 (m, 1 H, $C(4)NH_2$; 2 H, Ar); 7.12 (d, 2 H, Ar, ^3J = 7.0); 9.60 (br.s, 1 H, C(5)NH); 10.34 (s, 1 H, NH); 10.85 (br.s, 1 H, $C(4)NH_2$)
13c	3585—3150 (2 NH, 2 NH_2); 2195, 2178 sh (CN); 1680 (C=O)	2.61 (br.pseudod, 1 H, C(9)H, ^2J = 16.0)*; 2.92 (dd, 1 H, C(9)H, ^2J = 16.0, ^3J = 7.1); 5.01 (br.pseudod, 1 H, C(10)H)*; 6.36 (br.s, 2 H, $C(2)NH_2$); 6.90 (br.s, 1 H, $C(4)NH_2$); 7.12—7.23 (m, 5 H, Ph); 9.67 (br.s, 1 H, C(5)NH); 10.40 (s, 1 H, NH); 10.85 (br.s, 1 H, $C(4)NH_2$)
13d	3590—3200 (2 NH, 2 NH_2); 2190, 2183 sh (CN); 1686 (C=O)	2.48 (br.pseudod, 1 H, C(9)H, ^2J = 16.4)*; 2.86 (dd, 1 H, C(9)H, ^2J = 16.4, ^3J = 7.1); 3.68, 3.72 (both s, 3 H each, $(MeO)_2$); 4.92 (br.pseudod, 1 H, C(10)H)*; 6.44 (br.s, 2 H, $C(2)NH_2$); 6.65 (br.d, 2 H, Ar, ^3J = 8.2); 6.85 (br.s, 1 H, $C(4)NH_2$); 6.87 (s, 1 H, Ar); 9.66 (s, 1 H, C(5)NH); 10.37 (s, 1 H, NH); 10.85 (br.s, 1 H, $C(4)NH_2$)

* The doublet of doublets is resolved as a broadened pseudodoublet due to overlapping of the signals.

** The signal for the proton of the COOH group was not observed due to the deuterium exchange.

Table 2. Selected bond lengths (*d*) and bond angles (ω) in **13a**·2DMF

Bond	*d*/Å	Angle	ω/deg
Cl(1)—C(17)	1.738(3)	C(1)—S(1)—C(8)	104.87(12)
S(1)—C(1)	1.733(3)	C(1)—N(1)—C(2)	123.07(19)
S(1)—C(8)	1.779(2)	C(6)—N(2)—C(11)	118.81(18)
O(1)—C(2)	1.227(3)	S(1)—C(1)—C(5)	124.97(16)
N(1)—C(1)	1.399(3)	N(1)—C(1)—C(5)	122.36(19)
N(1)—C(2)	1.360(3)	N(1)—C(2)—C(3)	115.72(19)
N(2)—C(6)	1.346(3)	C(2)—C(3)—C(4)	114.74(18)
N(5)—C(9)	1.338(3)	C(1)—C(5)—C(6)	122.71(19)
N(6)—C(8)	1.271(3)	N(2)—C(6)—C(7)	124.03(17)
C(1)—C(5)	1.345(3)	C(5)—C(6)—C(7)	124.13(18)
C(2)—C(3)	1.495(3)	C(6)—C(7)—C(8)	123.26(17)
C(3)—C(4)	1.536(3)	S(1)—C(8)—C(7)	119.68(16)
C(4)—C(5)	1.505(3)	C(7)—C(9)—C(10)	117.62(18)
C(5)—C(6)	1.459(3)	C(9)—C(10)—C(11)	120.10(18)
C(6)—C(7)	1.405(3)	N(2)—C(11)—C(10)	122.19(19)
C(7)—C(8)	1.458(3)		
C(7)—C(9)	1.435(3)		
C(9)—C(10)	1.408(3)		
C(10)—C(11)	1.398(3)		

whose presence was confirmed by X-ray diffraction analysis of crystal solvate **13a**·2DMF.

The selected bond lengths and bond angles in this compound are given in Table 2. The overall view of molecule **13a** is shown in Fig. 1. The bicyclic S(1)N(2)C(1)C(5)—C(11) system is virtually planar, *viz.*, the deviations of the atoms from the mean plane are no larger than 0.071 Å and the S(1)—C(1)—C(5)—C(8)/N(2)—C(6)—C(7)—C(9)—C(11)

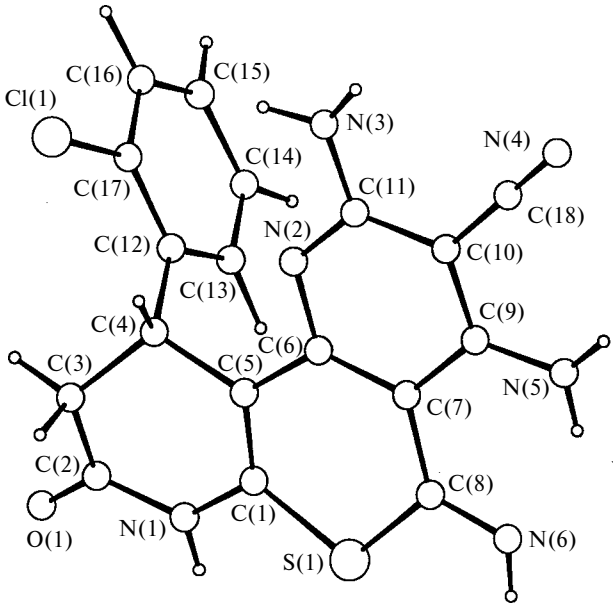


Fig. 1. Overall view and atomic numbering scheme for molecule **13a**.

dihedral angle is only 3.3°. By contrast, the N(1)—C(1)—C(5) ring is substantially nonplanar and adopts a distorted half-boat conformation (for this ring, the modified Cremer—Pople parameters[17] *S*, θ, and ψ are 0.52, 60.0°, and 15.6°, respectively). The N(1), N(3), and N(5) atoms in molecule **13a** have a planar-trigonal configuration (the sum of the bond angles at these atoms is 360° to within the experimental error). Due to efficient n—π conjugation, the N(3)—C(11) and N(5)—C(9) bond lengths (1.348(3) and 1.338(3) Å, respectively) are substantially smaller than the length of the standard $N(sp^2)$—$C(sp^2)$ single bond (1.45 Å [18]). The steric effects are responsible for the virtually orthogonal arrangement of the C(12)—C(17) benzene ring with respect to the heterocyclic system (the corresponding dihedral angle is 88.8°).

In the crystal of **13a**·2DMF, the intermolecular hydrogen bonds O(2)...H(1)—N(2) (O(2)...N(1), 2.823(3) Å; O(2)...H(1), 1.99(3) Å; O(2)—H(1)—N(1), 169(2)°), O(3)...H(5)—N(5) (O(3)...N(5), 3.005(3) Å; O(3)...H(5), 2.18(3) Å; O(3)—H(5)—N(5), 158(2)°), O(3)...H(6)—N(6) (O(3)...N(6), 3.015(3) Å; O(2)...H(1), 2.19(3) Å; O(2)—H(1)—N(1), 176(2)°), and N(3)—H(3)...N(4) (N(3)...N(4), 3.005(3) Å; N(4)...H(3), 2.19(3) Å; N(3)—H(3)—N(4), 165(2)°) form a two-dimensional network (Fig. 2). For reference, it should be noted that the average O...N and N...N distances in hydrogen bonds of the N—H...O, O—H...N, and N—H...N types are[19] 2.89, 2.79, and 2.98 Å, respectively.

The IR spectra of pyridothienopyridinones **4** have characteristic stretching bands of the $C(2)NH_2$ group and the endocyclic imino group (3550—3145 cm^{-1}) and absorption bands of the cyano and C=O groups in the regions of 2207—2196 and 1692—1670 cm^{-1}, respectively. The IR spectra of pyridothiopyranopyridinones **13** show broad stretching bands of two amino groups and two imino groups in the region of 3590—3150 cm^{-1}. The absorption bands corresponding to stretching vibrations of the cyano group are observed in the region of 2200—2190 cm^{-1}. The signals of the carbonyl group are observed at 1680—1686 cm^{-1} (see Table 1).

To summarize, we synthesized for the first time previously unknown heterocyclic systems, *viz.*, 6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridines and 7,8,9,10-tetrahydro-5*H*-pyrido[2′,3′:2,3]thiopyrano[4,5-*b*]pyridines, based on *N*-methylmorpholinium 4-aryl(hetaryl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates, malononitrile, or its derivatives. This fact provides evidence that multicomponent cascade heterocyclization holds promise for the synthesis of new fused heterocyclic systems.

Experimental

The ^1H NMR spectra were recorded on a Gemini 200 instrument (200 MHz) in DMSO-d_6 (for thiolates **1b—g,j,k**, in a

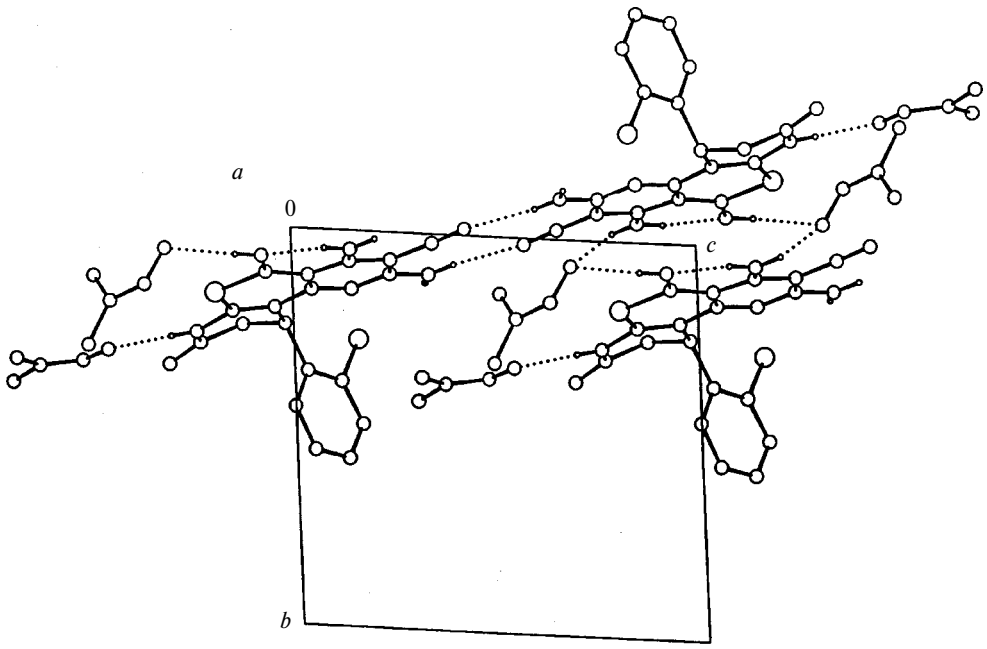


Fig. 2. Crystal packing of compound **13a** (intermolecular hydrogen bonds are indicated by dashed lines).

DMSO-d_6—CCl_4 mixture) with Me_4Si as the internal standard. The IR spectra were measured on an IKS-29 spectrophotometer in Nujol mulls. Elemental analysis for C, H, and N was carried out on a Perkin—Elmer C, H, N-analyser instrument. The course of the reactions and purities of the reaction products were monitored by TLC on Silufol UV-254 plates in the 3 : 5 acetone—hexane system; visualization was carried out with the use of iodine vapor. The melting points were determined on a Kofler stage.

***N*-Methylmorpholinium 4-(2-chlorophenyl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate (1a)** was synthesized according to a known procedure (method *A*).[12]

***N*-Methylmorpholinium 4-aryl(hetaryl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates 1b—g,j,k** were prepared analogously to thiolate **1a** (method *A*),[12] compounds **1i**[16] and **1h,l**[20] were synthesized according to procedures described earlier.

***N*-Methylmorpholinium 5-cyano-4-(1-naphthyl)-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate (1b).** The yield was 72.4%. M.p. 150 °C (decomp.). Found (%): C, 66.01; H, 6.19; N, 10.83. $C_{21}H_{23}N_3O_2S$. Calculated (%): C, 66.12; H, 6.08; N, 11.01. IR, ν/cm^{-1}: 3550—3260 (NH, NH^+); 2166 (CN); 1648 (C=O). ^{1}H NMR, δ: 2.43 (dd, 1 H, C(3)H, ^2J = 16.0 Hz, ^3J = 3.2 Hz); 2.80 (s, 3 H, NMe); 2.93 (dd, 1 H, C(3)H, ^2J = 16.0 Hz, ^3J = 7.5 Hz); 3.19 and 3.78 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 4.51 (m, 1 H, C(4)H); 7.34—8.11 (m, 7 H, Ar); 8.33 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-4-(4-ethoxyphenyl)-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate (1c).** The yield was 64.5%. M.p. 120 °C (decomp.). Found (%): C, 60.90; H, 6.81; N, 11.08. $C_{19}H_{25}N_3O_3S$. Calculated (%): C, 60.78; H, 6.71; N, 11.19. IR, ν/cm^{-1}: 3550—3250 (NH, NH^+); 2173 (CN); 1661 (C=O). ^{1}H NMR, δ: 1.33 (t, 3 H, $OCH_2C\underline{H}_3$, ^3J = 7.0 Hz); 2.34 (dd, 1 H, C(3)H, ^2J = 16.1 Hz, ^3J = 4.3 Hz); 2.69 (dd, 1 H, C(3)H, ^2J = 16.1 Hz, ^3J = 7.3 Hz); 2.77 (s, 3 H, NMe); 3.15 and 3.76 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.59 (m, 1 H, C(4)H); 3.97 (q, 2 H, $OC\underline{H}_2CH_3$, ^3J = 7.0 Hz); 6.79 and 7.07 (both d, 2 H each, Ar, ^3J = 8.6 Hz); 8.27 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-4-(3,4-dimethoxyphenyl)-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate (1d).** The yield was 70%. M.p. 135 °C (decomp.). Found (%): C, 58.42; H, 6.55; N, 10.60. $C_{19}H_{25}N_3O_4S$. Calculated (%): C, 58.29; H, 6.44; N, 10.73. IR, ν/cm^{-1}: 3555—3225 (NH, NH^+); 2174 (CN); 1654 (C=O). ^{1}H NMR, δ: 2.38 (dd, 1 H, C(3)H, ^2J = 15.6 Hz, ^3J = 3.6 Hz); 2.67 (dd, 1 H, C(3)H, ^2J = 15.6 Hz, ^3J = 6.4 Hz); 2.78 (s, 3 H, NMe); 3.16 and 3.80 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.59 (pseudot, 1 H, C(4)H); 3.74 and 3.76 (both s, 3 H each, $(MeO)_2$); 6.66—6.82 (m, 3 H, Ar); 8.10 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-4-(2,5-dimethoxyphenyl)-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate (1e).** The yield was 69.9%. M.p. 110 °C (decomp.). Found (%): C, 58.34; H, 6.51; N, 10.58. $C_{19}H_{25}N_3O_4S$. Calculated (%): C, 58.29; H, 6.44; N, 10.73. IR, ν/cm^{-1}: 3570—3270 (NH, NH^+); 2166 (CN); 1668 (C=O). ^{1}H NMR, δ: 2.32 (dd, 1 H, C(3)H, ^2J = 16.1 Hz, ^3J = 3.5 Hz); 2.64 (dd, 1 H, C(3)H, ^2J = 16.1 Hz, ^3J = 7.5 Hz); 2.77 (s, 3 H, NMe); 3.15 and 3.79 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.69 and 3.76 (both s, 3 H each, $(MeO)_2$); 3.89 (dd, 1 H, C(4)H, ^3J = 3.5 Hz, ^3J = 7.5 Hz); 6.61—6.85 (m, 3 H, Ar); 8.29 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-2-oxo-4-(*p*-tolyl)-1,2,3,4-tetrahydropyridine-6-thiolate (1f).** The yield was 71%. M.p. 130 °C (decomp.). Found (%): C, 62.77; H, 6.82; N, 12.31. $C_{18}H_{23}N_3O_2S$. Calculated (%): C, 62.58; H, 6.71; N, 12.16. IR, ν/cm^{-1}: 3540—3165 (NH, NH^+); 2170 (CN); 1662 (C=O). ^{1}H NMR, δ: 2.28 (s, 3 H, Me_{Ar}); 2.40 (dd, 1 H, C(3)H, ^2J = 16.0 Hz, ^3J = 4.3 Hz); 2.69 (dd, 1 H, C(3)H, ^2J = 16.0 Hz, ^3J = 7.2 Hz); 2.75 (s, 3 H, NMe); 3.11 and 3.76 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.60 (m, 1 H, C(4)H); 7.06 (br.s, 4 H, Ar); 8.23 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-2-oxo-4-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydropyridine-6-thiolate (1g).** The yield was 66.5%. M.p. 145 °C (decomp.). Found (%): C, 57.32; H, 6.37; N, 10.08. $C_{20}H_{27}N_3O_5S$. Calculated (%): C, 56.99; H, 6.46; N, 9.97. IR, ν/cm^{-1}: 3550—3260 (NH, NH$^+$); 2160 (CN); 1670 (C=O). ^{1}H NMR, δ: 2.40 (dd, 1 H, C(3)H, ^2J = 16.2 Hz, ^3J = 4.8 Hz); 2.67 (dd, 1 H, C(3)H, ^2J = 16.2 Hz, ^3J = 7.0 Hz); 2.77 (s, 3 H, NMe); 3.15 and 3.82 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.60 (m, 1 H, C(4)H); 3.65 (s, 3 H, MeO); 3.76 (s, 6 H, $(MeO)_2$); 6.45 (s, 2 H, Ar); 8.19 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-4-(3,4-methylenedioxyphenyl)-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate (1j).** The yield was 79.2%. M.p. 140 °C (decomp.). Found (%): C, 57.89; H, 5.71; N, 11.01. $C_{18}H_{21}N_3O_4S$. Calculated (%): C, 57.58; H, 5.64; N, 11.19. IR, ν/cm^{-1}: 3515—3210 (NH, NH$^+$); 2169 (CN); 1677 (C=O). ^{1}H NMR, δ: 2.31 (dd, 1 H, C(3)H, ^2J = 15.9 Hz, ^3J = 4.5 Hz); 2.68 (dd, 1 H, C(3)H, ^2J = 15.9 Hz, ^3J = 7.2 Hz); 2.78 (s, 3 H, NMe); 3.17 and 3.77 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.57 (m, 1 H, C(4)H); 5.94 (br.s, 2 H, OCH_2O); 6.61—6.78 (m, 3 H, Ar); 8.38 (br.s, 1 H, NH).

***N*-Methylmorpholinium 5-cyano-2-oxo-4-phenyl-1,2,3,4-tetrahydropyridine-6-thiolate (1k).** The yield was 67%. M.p. 120 °C (decomp.). Found (%): C, 61.39; H, 6.50; N, 12.76. $C_{17}H_{21}N_3O_2S$. Calculated (%): C, 61.61; H, 6.39; N, 12.68. IR, ν/cm^{-1}: 3525—3270 (NH, NH$^+$); 2167 (CN); 1665 (C=O). ^{1}H NMR, δ: 2.36 (dd, 1 H, C(3)H, ^2J = 15.9 Hz, ^3J = 3.7 Hz); 2.72 (dd, 1 H, C(3)H, ^2J = 15.9 Hz, ^3J = 7.1 Hz); 2.78 (s, 3 H, NMe); 3.16 and 3.76 (both m, 4 H each, CH_2NCH_2 and CH_2OCH_2); 3.65 (m, 1 H, C(4)H); 7.16—7.29 (m, 5 H, Ph); 8.26 (br.s, 1 H, NH).

Synthesis of pyridothienopyridones 4a—j (general procedure). ***A.*** A mixture of the corresponding pyridinethiolate **1** (8.2 mmol), nitrile **2** (0.81 g, 12.3 mmol), and acetone **3** (6 mL, 82 mmol) in EtOH (35 mL) was refluxed with stirring for 15—20 h (in the case of **4b,g,j**, for 25 h). Then the reaction mixture was kept at ~20 °C for 48 h. The reaction product was filtered off and purified by recrystallization from the corresponding solvent.

2-Amino-9-(2-chlorophenyl)-3-cyano-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4a). The synthesis according to the method *A* has been described earlier.[9]

B. A mixture of Michael adduct **5** (4 g, 8.5 mmol), acetone **3** (6.3 mL, 85 mmol), and nitrile **2** (1.13 g, 17 mmol) was refluxed in EtOH (35 mL) for 35 h and then kept at ~20 °C for 48 h. The precipitate that formed was filtered off and recrystallized from AcOH to obtain pyridothienopyridone **4a** in a yield of 0.58 g (18.5%).

C. A mixture of 2-chlorobenzaldehyde (**6**) (2.27 mL, 20 mmol) and cyanothioacetamide (**7**) (2 g, 20 mmol) in EtOH (70 mL) in the presence of two drops of *N*-methylmorpholine (**9**) was stirred for 1 h. Then Meldrum′s acid (**8**) (2.88 g, 20 mmol) was added. *N*-Methylmorpholine (**9**) (3.3 mL, 30 mmol) was added dropwise with stirring. After 10 min, nitrile **2** (2.64 g, 40 mol) and acetone (**3**) (14.7 mL, 0.2 mol) were added to the precipitate of the Michael adduct that formed. The reaction mixture was refluxed for 10 days. The crystals that precipitated were filtered off and recrystallized from AcOH to obtain pyridothienopyridone **4a** in a yield of 0.52 g (7%).

D. A mixture of thiolate **1a** (2 g, 5.5 mmol), isopropylidenemalononitrile (**10**) (0.87 g, 8.2 mmol), and acetone (5 mL) in EtOH (30 mL) was refluxed for 20 h and then kept at ~20 °C for 48 h. The crystalline precipitate was filtered off and recrystallized from the corresponding solvent to obtain pyridothienopyridone **4a** in a yield of 0.67 g (33%).

Recrystallization from a 1 : 1 EtOH—AcOH mixture afforded the 1 : 1 solvate with EtOH, m.p. 283—285 °C (decomp.), which was studied by X-ray diffraction analysis;[9] the nonsolvated product precipitated from AcOH, m.p. 297—298 °C. The spectroscopic characteristics and data from elemental analysis of pyridothienopyridone **4a** prepared according to the methods *B*, *C*, and *D* are identical with those reported earlier.[9]

2-Amino-3-cyano-4-methyl-9-(1-naphthyl)-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4b). The yield was 36%. T.decomp. > 310 °C (from AcOH), yellow crystals. Found (%): C, 68.88; H, 4.25; N, 14.48. $C_{22}H_{16}N_4OS$. Calculated (%): C, 68.73; H, 4.19; N, 14.57.

2-Amino-3-cyano-9-(4-ethoxyphenyl)-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4c). The yield was 30.4%. M.p. 262—263 °C (from EtOH—AcOH, 2 : 1), pale-yellow crystals. Found (%): C, 63.88; H, 4.85; N, 14.88. $C_{20}H_{18}N_4O_2S$. Calculated (%): C, 63.47; H, 4.79; N, 14.80.

2-Amino-3-cyano-9-(3,4-dimethoxyphenyl)-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4d). The yield was 38%. T.decomp. > 298 °C (from EtOH—AcOH, 1 : 1), pale-yellow crystals. Found (%): C, 61.33; H, 4.66; N, 14.40. $C_{20}H_{18}N_4O_3S$. Calculated (%): C, 60.90; H, 4.60; N, 14.20.

2-Amino-3-cyano-9-(2,5-dimethoxyphenyl)-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4e). The yield was 35%. M.p. 336—338 °C (from EtOH—AcOH, 1 : 2), pale-yellow crystals. Found (%): C, 61.30; H, 4.66; N, 14.33. $C_{20}H_{18}N_4O_3S$. Calculated (%): C, 60.90; H, 4.60; N, 14.20.

2-Amino-3-cyano-4-methyl-7-oxo-9-(*p*-tolyl)-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4f). The yield was 34%. M.p. 288—290 °C (from EtOH—AcOH, 1 : 3), pale-yellow crystals. Found (%): C, 65.02; H, 4.70; N, 16.24. $C_{19}H_{16}N_4OS$. Calculated (%): C, 65.50; H, 4.63; N, 16.08.

2-Amino-3-cyano-4-methyl-7-oxo-9-(3,4,5-trimethoxyphenyl)-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4g). The yield was 28%. M.p. 276—278 °C (from AcOH), finely crystalline white powder. Found (%): C, 59.60; H, 4.67; N, 13.31. $C_{21}H_{20}N_4O_4S$. Calculated (%): C, 59.42; H, 4.75; N, 13.20.

2-Amino-3-cyano-4-methyl-7-oxo-9-(2-thienyl)-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4h) (solvate with AcOH (1 : 1)). The yield was 27%. M.p. 297—299 °C (from AcOH), pale-yellow crystals. Found (%): C, 54.22; H, 4.08; N, 14.15. $C_{18}H_{16}N_4O_3S_2$. Calculated (%): C, 53.99; H, 4.03; N, 13.99.

2-Amino-3-cyano-9-(2-methoxyphenyl)-4-methyl-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4i). The yield was 29%. M.p. 325—327 °C (from AcOH), white powder. Found (%): C, 63.01; H, 4.47; N, 15.60. $C_{19}H_{16}N_4O_2S$. Calculated (%): C, 62.62; H, 4.43; N, 15.37.

2-Amino-3-cyano-4-methyl-9-(3,4-methylenedioxyphenyl)-7-oxo-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4j). The yield was 30%. M.p. 276—278 °C (from AcOH—EtOH, 4 : 1), colorless crystals. Found (%): C, 60.40; H, 3.77; N, 14.84. $C_{19}H_{14}N_4O_3S$. Calculated (%): C, 60.31; H, 3.73; N, 14.81.

2-Amino-3-cyano-4-methyl-7-oxo-9-phenyl-6,7,8,9-tetrahydropyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine (4k). The yield

was 51%. M.p. 316 °C (from EtOH—AcOH, 1 : 1), colorless crystals. Found (%): C, 64.90; H, 4.27; N, 16.87. $C_{18}H_{14}N_4OS$. Calculated (%): C, 64.65; H, 4.22; N, 16.75.

Synthesis of pyridothiopyranopyridones 13 (general procedure). ***A.*** A mixture of the corresponding thiolate **1a,l** (4 mmol) and nitrile **2** (0.79 g, 12 mmol) in EtOH (30 mL) was refluxed for 25 h. The precipitate was filtered off and recrystallized from the corresponding solvent.

B. A suspension of the corresponding thiolate **1a,d,k** (9 mmol) and 2-amino-1,1,3-tricyanopropene (**14**) (1.78 g, 13.5 mmol) in EtOH (35 mL) was refluxed for 15 h. The precipitate that formed was filtered off and recrystallized from the corresponding solvent.

2,4-Diamino-10-(2-chlorophenyl)-3-cyano-5-imino-8-oxo-7,8,9,10-tetrahydro-5*H*-pyrido[2′,3′:2,3]thiopyrano[4,5-*b*]pyridine (13a). The yields according to the methods *A* and *B* were 29 and 44%, respectively. T.decomp. > 325 °C (from AcOH—DMF, 1 : 1), yellow-green crystals. Found (%): C, 54.75; H, 3.33; N, 21.28. $C_{18}H_{13}ClN_6OS$. Calculated (%): C, 54.48; H, 3.30; N, 21.18. MS (EI, 70 eV), *m/z* (I_{rel} (%)): 396 $[M]^+$ (100), 365 (43), 363 (82), 361 (62), 261 (60), 165 (57), 101 (47). Crystals of solvate **13a**·2DMF suitable for X-ray diffraction analysis were grown from DMF.

2,4-Diamino-3-cyano-5-imino-10-(4-methoxyphenyl)-8-oxo-7,8,9,10-tetrahydro-5*H*-pyrido[2′,3′:2,3]thiopyrano[4,5-*b*]pyridine (13b). The yield according to the method *A* was 25%. T.decomp. 288—291 °C (from AcOH—DMF, 1 : 1), dark-yellow crystals. Found (%): C, 58.34; H, 4.15; N, 21.64. $C_{19}H_{16}N_6O_2S$. Calculated (%): C, 58.15; H, 4.11; N, 21.41.

2,4-Diamino-3-cyano-5-imino-8-oxo-10-phenyl-7,8,9,10-tetrahydro-5*H*-pyrido[2′,3′:2,3]thiopyrano[4,5-*b*]pyridine (13c). The yield according to the method *B* was 40%. M.p. 280—282 °C (from AcOH), brown crystals. Found (%): C, 59.99; H, 3.93; N, 23.32. $C_{18}H_{14}N_6OS$. Calculated (%): C, 59.66; H, 3.89; N, 23.19.

2,4-Diamino-3-cyano-10-(3,4-dimethoxyphenyl)-5-imino-8-oxo-7,8,9,10-tetrahydro-5*H*-pyrido[2′,3′:2,3]thiopyrano[4,5-*b*]pyridine (13d). The yield according to the method *B* was 53%. M.p. 284—286 °C (from AcOH), yellow-brown crystals. Found (%): C, 57.12; H, 4.23; N, 19.98. $C_{20}H_{18}N_6O_3S$. Calculated (%): C, 56.86; H, 4.29; N, 19.89. MS (EI, 70 eV), *m/z* (I_{rel} (%)): 422 $[M]^+$ (100), 389 (46), 308 (30), 264 (27), 191 (96), 160 (20), 77 (19).

X-ray diffraction study of compound 13a was carried out on an automated four-circle Enraf—Nonius CAD-4 diffractometer (Cu-Kα radiation, the ratio between the scan rates $2\theta/\omega = 1.2$, $\theta_{max} = 65°$) at ~20 °C. The structure was solved by direct methods and refined anisotropically by the full-matrix least-squares method with the use of the CRYSTALS program package.[21] All H atoms were revealed from the difference electron density synthesis and included in the refinement with fixed positional and thermal parameters (only the H(1)—H(4) atoms were refined isotropically). The absorption correction was applied using the azimuthal scanning method.[22] The Chebyshev weighting scheme[23] was used in the refinement. The selected bond lengths and bond angles are listed in Table 2. The principal crystallographic data and details of X-ray diffraction study and refinement are given in Table 3. The complete crystallographic data, including the atomic coordinates, were deposited with the Cambridge Structural Database.

Table 3. Principal crystallographic data and details of X-ray diffraction study and refinement of compound **13a**·2DMF

Parameter	Characteristic
Molecular formula	$C_{24}H_{27}ClN_8O_3S$
Molecular weight	543.05
a/Å	9.834(8)
b/Å	11.451(10)
c/Å	12.167(9)
α/deg	83.75(8)
β/deg	79.17(6)
γ/deg	82.09(8)
V/Å^3	1323.9
Z	2
d_{calc}/g cm^{-3}	1.36
Space group	$P\bar{1}$ (No. 2)
μ/cm^{-1}	23.5
F(000)	570.8
Crystal dimensions/mm	0.40×0.50×0.50
Segment of the sphere	$0 < h < 11$
	$-13 < k < 13$
	$-14 < l < 14$
Number of reflections	
measured	4501
independent	4487
in least-squares ($I > 3\sigma(I)$)	4006
R_{int}	0.018
Number of refinable parameters	358
Number of reflections per parameter	11.1
R	0.046
R_w	0.053
GOF	1.073
Weighting coefficients	4.47, −0.52, 2.63, −0.84
Δρ/e cm^{-3}	0.42/−0.55

This study was financially supported by the Russian Foundation for Basic Research (Project No. 02-03-32063).

References

1. V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 1998, 2123 [*Russ. Chem. Bull.*, 1998, **47**, 2053 (Engl. Transl.)].
2. A. S. Fisyuk and Yu. G. Bundel′, *Khim. Geterotsikl. Soedin.*, 1999, 147 [*Chem. Heterocycl. Compd.,* 1999 (Engl. Transl.)].
3. S. G. Krivokolysko, Ph. D. (Chem.) Thesis, Institute of Organic Chemistry of the Russian Academy of Sciences, Moscow, 1997, 215 pp. (in Russian).
4. C. G. Krivokolysko, Dr. Sc. (Chem.) Thesis, Moscow State University, Moscow, 2001, 346 pp. (in Russian).
5. V. P. Litvinov, V. K. Promonenkov, Yu. A. Sharanin, and A. M. Shestopalov, in *Itogi nauki i tekhniki. Organicheskaya khimiya* [*Advances in Science and Technology. Organic Chemistry*], VINITI, Moscow, 1989, **17**, 72 (in Russain).

6. V. P. Litvinov, S. G. Krivokolysko, and V. D. Dyachenko, *Khim. Geterotsikl. Soedin.*, 1999, 579 [*Chem. Heterocycl. Compd.,* 1999 (Engl. Transl.)].
7. A. Krauze and G. Duburs, *Khim. Geterotsikl. Soedin.*, 2001, 404 [*Chem. Heterocycl. Compd.,* 2001 (Engl. Transl.)].
8. N. A. Ismail, S. M. Eldin, F. A. Attaby, and V. B. A. Abo-Abdou, *Pak. J. Sci. Ind. Res.*, 1992, 165; *Chem. Abstrs.,* 1993, **118**, 233980q.
9. V. V. Dotsenko, S. G. Krivokolysko, V. P. Litvinov, and A. N. Chernega, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 339 [*Russ. Chem. Bull.*, *Int. Ed.*, 2002, **51**, 362].
10. V. A. Artemov, V. L. Ivanov, L. A. Rodinovskaya, A. M. Shestopalov, and V. P. Litvinov, *Khim. Geterotsikl. Soedin.*, 1996, 553 [*Chem. Heterocycl. Compd.,* 1996 (Engl. Transl.)].
11. M. P. Goncharenko, Yu. A. Sharanin, and A. V. Turov, *Zh. Org. Khim.*, 1993, **29**, 1610 [*Russ. J. Org. Chem.*, 1993, **29** (Engl. Transl.)].
12. V. N. Nesterov, S. G. Krivokolysko, V. D. Dyachenko, V. V. Dotsenko, and V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 1029 [*Russ. Chem. Bull.*, 1997, **46**, 990 (Engl. Transl.)].
13. *Chemistry of Organosulfur Compounds. General Problems*, Ed. L. I. Belen´kii, Ellis Horwood, Chichester, UK, 1990, 378 pp.
14. F. S. Babichev, Yu. A. Sharanin, V. P. Litvinov, V. K. Promonenkov, and Yu. M. Volovenko, *Vnutrimolekulyarnoe vzaimodeistvie nitril´noi i C—H-, O—H- i S—H-grupp* [*Intramolecular Interactions of the Nitrile Group with the C—H, O—H, and S—H Groups*], Naukova Dumka, Kiev, 1985, p. 124 (in Russian).
15. S. G. Krivokolysko, V. D. Dyachenko, and V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 2333 [*Russ. Chem. Bull.*, 1999, **48**, 2308 (Engl. Transl.)].
16. S. G. Krivokolysko, V. D. Dyachenko, and V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 485 [*Russ. Chem. Bull.*, *Int. Ed.*, 2000, **49**, 487].
17. N. S. Zefirov and V. A. Palyulin, *Dokl. Akad. Nauk SSSR,* 1980, **252**, 111 [*Dokl. Chem.*, 1980 (Engl. Transl.)].
18. M. Burke-Laing and M. Laing, *Acta Crystallogr., Sect. B,* 1976, **32**, 3216.
19. L. N. Kuleshova and P. M. Zorkii, *Acta Crystallogr.*, *Sect. B*, 1981, **37**, 1363.
20. V. D. Dyachenko, S. G. Krivokolysko, and V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 1852 [*Russ. Chem. Bull.*, 1997, **46**, 1758 (Engl. Transl.)].
21. D. J. Watkin, C. K. Prout, J. R. Carruthers, and P. W. Betteridge, *CRYSTALS, Issue 10*, Chemical Crystallography Laboratory, University of Oxford, 1996.
22. A. C. T. North, D. C. Phillips, F. Scott, and F. S. Mathews, *Acta Crystallogr.*, *Sect. A*, 1968, **24**, 351.
23. J. R. Carruthers and D. J. Watkin, *Acta Crystallogr., Sect. A,* 1979, **35**, 698.

Received June 20, 2002;
in revised form November 28, 2002