Anilinomethylidene derivatives of cyclic 1,3-dicarbonyl compounds in the synthesis of new sulfur-containing pyridines and quinolines

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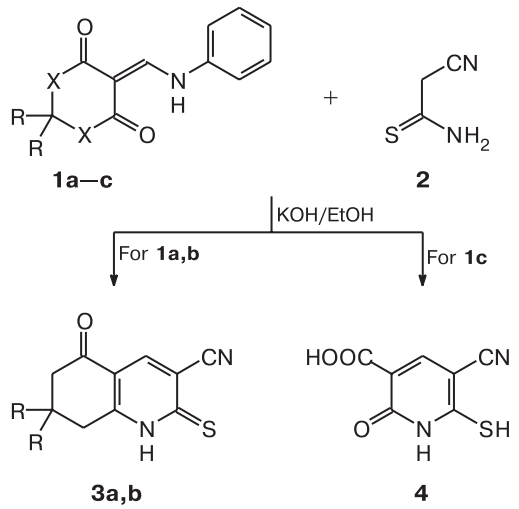
Simple methods for the synthesis of previously unknown sulfur-containing pyridin-2-ones and 5,6,7,8-tetrahydroquinolines from cyanothioacetamide and anilinomethylidene derivatives of cyclic 1,3-dicarbonyl compounds were developed. Structures and chemical transformations of compounds obtained were studied.

Key words: pyridinones, tetrahydroquinolines, alkylation, bromination, X-ray diffraction analysis.

Derivatives of sulfur-containing pyridines and quinolines possess a rather broad spectrum of useful biological activity.[1,2] At the same time, the progress in this area of heterocyclic chemistry is impeded by a limited number of methods for their synthesis, which in turn is due to the fact that the starting substrates and reagents are difficultly accessible. Aiming at the development of convenient methods for the synthesis of functionalized azines based on cascade heterocyclization and multi-component condensation of simple and accessible reagents,[3] we studied the reactions of cyanothioacetamide with anilinomethylidene derivatives of cyclic 1,3-dicarbonyl compounds **1a**—**c**.

Scheme 1



R = H, X = CH_2 (**a**); R = Me, X = CH_2 (**b**); R = Me, X = O (**c**)

Results and Discussion

Reactions of diketones **1a,b** with thioamide **2** in EtOH in the presence of KOH at 20 °C afford the corresponding thiones **3** in 80—82% yield, while Meldrum´s acid derivative **1c** reacts with compound **2** to give acid **4** in 64% yield (Scheme 1).

Reactions of compounds **3** with alkyl halides **5a**—**c** yielded sulfides **6**. In the case of compounds **5d**—**f** having an active methylene group, the corresponding sulfides **6** undergo the *in situ* Thorpe—Ziegler cyclization into thieno[2,3-*b*]quinolines **7** (Scheme 2).

Like 3-cyano-1,2,5,6,7,8-hexahydroquinoline-2,5-dione,[4] compound **6b** is brominated in MeOH at position 6 of the tetrahydroquinoline ring to give bromide **8** (see Scheme 2).

Alkylation of thiol **4** with halides **5** in aqueous ethanol in the presence of KOH is also highly *S*-regioselective to give substituted pyridinones **9** and **10** as the reaction products (Scheme 3). Heating of the pyridine derivative **9d** with I_2 in EtOH yields 90% of dihydrothiazo-

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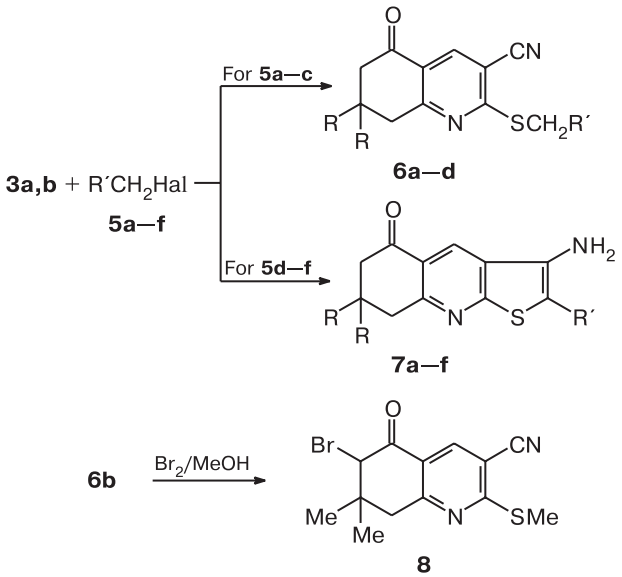
Scheme 2



5	**a**	**b**	**c**	**d**	**e**	**f**
Hal	I	Cl	Br	Cl	Cl	Br
R′	H	Ph	Me	$CONH_2$	CONHPh	Bz

6	**a**	**b**	**c**	**d**
R	H	Me	Me	Me
R′	H	H	Ph	Me

7	**a**	**b**	**c**	**d**	**e**	**f**
R	H	H	H	Me	Me	Me
R′	$CONH_2$	CONHPh	Bz	$CONH_2$	CONHPh	Bz

lo[3,2-*a*]pyridine **11**. Oxidation of compound **4** with H_2O_2 under mild conditions gives disulfide **12**.

The structure of product **11** was proved unambiguously by X-ray diffraction analysis (Fig. 1). Selected bond lengths and angles are given in Table 1. The bicyclic S(1)N(1)C(1)—C(7) system can be regarded as approximately planar since the deviations of the atoms from the mean-square plane reach 0.14 Å. The five-membered

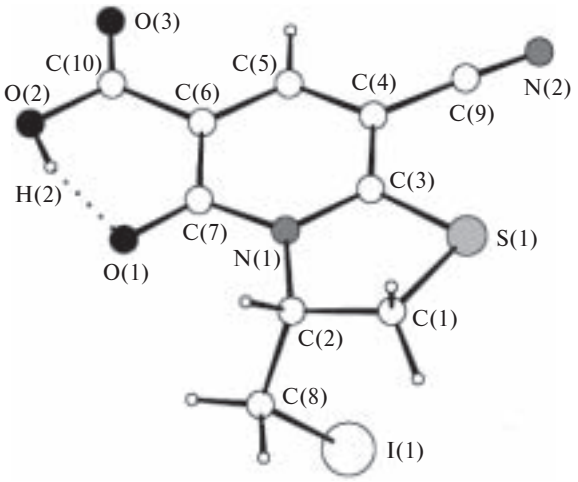
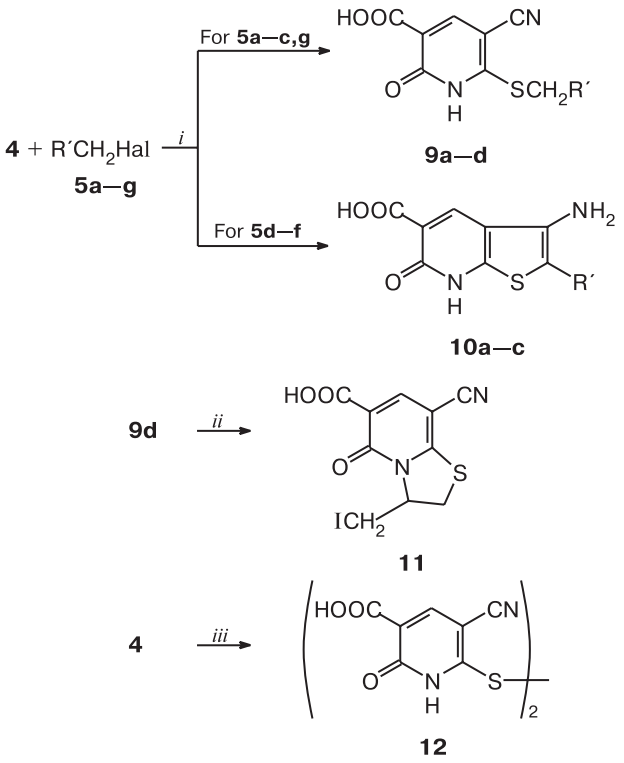


Fig. 1. General view of structure **11** with the numbering of nonhydrogen atoms.

Scheme 3



5g: R′ = $CH=CH_2$, Hal = Br (R′ and Hal for **5a—f** see Scheme 2)

9	**a**	**b**	**c**	**d**	**10**	**a**	**b**	**c**
R′	H	Ph	Me	$CH=CH_2$	R′	$CONH_2$	CONHPh	Bz

Reagents and conditions: *i*. KOH/EtOH. *ii*. I_2/EtOH, Δ. *iii*. H_2O_2, KOH, 50% EtOH, 20 °C.

Table 1. Selected bond lengths (*d*) and angles (ω) in compound **11**

Bond	*d*/Å	Angle	ω/deg
I(1)—C(8)	2.136(5)	C(1)—S(1)—C(3)	92.5(3)
S(1)—C(1)	1.822(5)	C(2)—N(1)—C(3)	115.6(4)
S(1)—C(3)	1.712(5)	C(2)—N(1)—C(7)	121.0(4)
O(1)—C(7)	1.241(6)	C(3)—N(1)—C(7)	123.4(4)
O(2)—C(10)	1.341(6)	S(1)—C(1)—C(2)	108.1(4)
O(3)—C(10)	1.197(6)	N(1)—C(2)—C(1)	107.4(4)
N(1)—C(2)	1.489(6)	S(1)—C(3)—N(1)	114.4(3)
N(1)—C(3)	1.356(6)	N(1)—C(3)—C(4)	120.0(4)
N(1)—C(7)	1.396(6)	C(3)—C(4)—C(5)	119.0(4)
C(1)—C(2)	1.525(8)	C(4)—C(5)—C(6)	121.7(4)
C(3)—C(4)	1.389(7)	C(5)—C(6)—C(7)	119.9(4)
C(4)—C(5)	1.382(7)	N(1)—C(7)—C(6)	116.0(4)
C(5)—C(6)	1.373(7)	N(2)—C(9)—C(4)	177.4(5)
C(6)—C(7)	1.442(7)		
C(6)—C(10)	1.491(7)		

heterocycle has a substantially flattened envelope conformation with a dihedral angle of 14.1° between the S(1)C(1)C(2) fragment and the S(1)C(3)N(1)C(2) plane. The interatomic S(1)—C(1) (1.822(5) Å) and S(1)—C(3) (1.712(5) Å) distances are typical of the S—C_{sp^3} and S—C_{sp^2} bonds, respectively.[5,6] The bond configuration at the N(1) atom is planar trigonal; the sum of the N(1) bond angles is 360.0(1.2)°. The geometrical parameters of the six-membered N(1)C(3)—C(7) ring indicate a significant electron density delocalization.[5,7] Structure **11** contains a rather strong[8] intramolecular hydrogen O(2)—H(2)...O(1) bond (O(1)...O(2) 2.565(6) Å, O(1)...H(2) 1.64(7) Å, O(2)—H(2) 0.97(7) Å, the O(1)—H(2)—O(2) angle 158(3)°).

Table 2. Spectral characteristics of compounds **3**, **4**, and **6—12**

Compound	IR, ν/cm^{-1}	^{1}H NMR, δ (J/Hz)
3a	3170, 3090, 3070 (NH); 2224 (CN); 1660 (C=O)	2.07, 2.56, 3.05 (all m, 6 H, $(CH_2)_3$); 8.14 (s, 1 H, H(4)); 14.15 (br.s, 1 H, NH)
3b	3185, 3128, 3060 (NH); 2228 (CN); 1660 (C=O)	1.05 (s, 6 H, 2 Me); 2.44, 2.93 (both br.s, 2 H each, $(CH_2)_2$); 8.28 (s, 1 H, H(4)); 14.31 (br.s, 1 H, NH)
4	3230—3030 (NH, OH); 2227 sh, 2216 (CN); 1675, 1680 (2 C=O)	7.89 (s, 1 H, H(4)); 11.95 (br.s, 1 H, NH); 13.93 (br.s, 1 H, COOH)[a]
6a	2228 (CN); 1690 (C=O)	2.16, 2.63, 3.13 (all m, 6 H, $(CH_2)_3$); 2.67 (s, 3 H, SMe); 8.30 (s, 1 H, H(4))
6b	2227 (CN); 1686 (C=O)	1.07 (s, 6 H, 2 Me); 2.53, 3.11 (both br.s, 2 H each, $(CH_2)_2$); 2.66 (s, 3 H, SMe); 8.32 (s, 1 H, H(4))
6c	2224 (CN); 1687 (C=O)	1.11 (s, 6 H, 2 Me); 2.55, 3.12 (both br.s, 2 H each, $(CH_2)_2$); 4.56 (br.s, 2 H, SCH_2); 7.28 (m, 3 H, Ar); 7.35 (m, 2 H, Ar); 8.34 (s, 1 H, H(4))
6d	2218 (CN); 1687 (C=O)	1.10 (s, 6 H, 2 Me); 1.42 (t, 3 H, $SCH_2C\underline{H}_3$, ^3J = 7.4); 2.53, 3.03 (both br.s, 2 H each, $(CH_2)_2$); 3.31 (q, 2 H, SCH_2, ^3J = 7.4); 8.30 (s, 1 H, H(4))
7a	3415, 3375, 3245 (2 NH_2); 1690, 1650 (2 C=O)	2.20, 2.68, 3.18 (all m, 6 H, $(CH_2)_3$); 6.95, 7.30 (both br.s, 2 H each, NH_2, $CONH_2$); 8.94 (s, 1 H, H(4))
7b	3420, 3357, 3295 (NH_2, NH); 1675, 1624 (2 C=O)	2.23, 2.72, 3.17 (all m, 6 H, $(CH_2)_3$); 7.07, 7.30 (both m, 3 H, Ar); 7.54 (br.s, 2 H, NH_2); 7.72 (d, 2 H, Ar, ^3J = 7.7); 9.05 (s, 1 H, H(4)); 9.35 (s, 1 H, NHCO)
7c	3355, 3235, 3170 (NH_2); 1675 (2 C=O)	2.20, 2.70, 3.15 (all m, 6 H, $(CH_2)_3$); 7.51, 7.75 (both m, 5 H, Ar); 8.54 (br.s, 2 H, NH_2); 9.17 (s, 1 H, H(4))
7d	3440, 3265, 3150 (2 NH_2); 1676, 1641 (2 C=O)	1.11 (s, 6 H, 2 Me); 2.57, 3.12 (both br.s, 2 H each, $(CH_2)_2$); 6.97, 7.30 (both br.s, 2 H each, NH_2, $CONH_2$); 8.93 (s, 1 H, H(4))
7e	3410—3280 (NH_2, NH); 1670, 1632 (2 C=O)	1.13 (s, 6 H, 2 Me); 2.60, 3.14 (both br.s, 2 H, $(CH_2)_2$); 7.03, 7.28 (both m, 3 H, Ar); 7.52 (br.s, 2 H, NH_2); 7.71 (d, 2 H, Ar, ^3J = 8.1); 9.02 (s, 1 H, H(4)); 9.31 (s, 1 H, NHCO)
7f	3335, 3235, 3100 (NH_2); 1673 (2 C=O)	1.13 (s, 6 H, 2 Me); 2.58, 3.08 (both br.s, 2 H each, $(CH_2)_2$); 7.50, 7.77 (both m, 5 H, Ar); 8.54 (br.s, 2 H, NH_2); 9.19 (s, 1 H, H(4))
8	2225 (CN); 1688 (C=O)	1.15, 1.23 (both s, 3 H each, 2 Me); 2.65 (s, 3 H, SMe); 2.96, 3.19 (both d, 2 H, $H_2C(8)$, ^2J = 18.0); 4.59 (s, 1 H, H(6)); 8.38 (s, 1 H, H(4))
9a	3420, 3210—3000 (NH, OH); 2223 (CN); 1735, 1682 (2 C=O)	2.65 (s, 3 H, SMe); 8.33 (s, 1 H, H(4))[b]
9b	3430, 3240—3050 (NH, OH); 2228 (CN); 1708, 1640 (2 C=O)	4.52 (br.s, 2 H, SCH_2); 7.27 (m, 3 H, Ar); 7.42 (m, 2 H, Ar); 8.31 (s, 1 H, H(4))[b]
9c	3395, 3240—3100 (NH, OH); 2227 (CN); 1725, 1690 (2 C=O)	1.40 (t, 3 H, $SCH_2C\underline{H}_3$, ^3J = 7.4); 3.27 (q, 2 H, SCH_2, ^3J = 7.4); 8.30 (s, 1 H, H(4))[b]
9d	3415, 3270—3100 (NH, OH); 2222 (CN); 1723, 1688 (2 C=O)	3.95 (br.d, 2 H, SCH_2, ^3J = 7.0); 5.16 (d, 1 H, *cis*-$C\underline{H}_2$=CH, ^3J = 10.0); 5.37 (d, 1 H, *trans*-$C\underline{H}_2$=CH, ^3J = 17.5); 5.93 (m, 1 H, $C\underline{H}$=CH_2); 8.33 (s, 1 H, H(4))[b]

(*to be continued*)

Table 2 (*continued*)

Compound	IR, ν/cm^{-1}	^{1}H NMR, δ (*J*/Hz)
10a	3435, 3355, 3315—3050 (2 NH_2, OH, NH); 1740, 1675, 1648 (3 C=O)	6.86 (br.s, 2 H, NH_2); 7.31, 7.34 (both br.s, 2 H, $CONH_2$); 9.12 (s, 1 H, H(4))[b]
10b	3420, 3340, 3310, 3210—3050 (2 NH, NH_2, OH); 1738, 1625 (3 C=O)	7.00 (t, 1 H, Ph, ^3J = 7.3); 7.25 (dd, 2 H, Ph, ^3J = 7.3, ^3J = 7.9); 7.64 (m, 4 H, NH_2, Ph); 9.18, 9.20 (both s, 1 H each, H(4), CONH)[b]
10c	3390, 3322, 3210—3060 (NH_2, NH, OH); 1725, 1633 (3 C=O)	7.49 (m, 3 H, Ph); 7.66 (d, 2 H, Ph, ^3J = 7.6); 8.51 (br.s, 2 H, NH_2); 9.28 (s, 1 H, H(4))[b]
11	3460—3050 (OH); 2227 sh, 2217 (CN); 1740, 1690 (2 C=O)	3.58—4.10 (m, 4 H, SCH_2, CH_2I); 5.43 (m, 1 H, H(3)); 8.33 (s, 1 H, H(7))[c]
12	3420, 3368, 3195—3040 (2 NH, 2 OH); 2230, 2215 sh. (2 CN); 1715, 1653 (4 C=O)	8.00 (s, 2 H, 2 H(4)); 10.87 (br.s, 2 H, 2 NHCO); 13.93 (br.s, 2 H, 2 COOH)

[a] No signal for the SH group appears because of deuterium exchange.
[b] No signals for the COOH and NH groups appear because of deuterium exchange.
[c] No signal for the COOH group appears because of deuterium exchange.

The structures of products **3**, **4**, and **6—12** were determined from the data of physicochemical studies (see Experimental and Table 2).

Experimental

^{1}H NMR spectra were recorded on Gemini 200 (200 MHz), Bruker DRX-500 (500 MHz) (for **3b**), and Bruker AM-300 (300 MHz) (for **4**) instruments in DMSO-d_6 with Me_4Si as the internal standard. IR spectra were recorded in Nujol on an IKS-29 spectrophotometer. Elemental analysis for C, H, and N was performed on a Perkin—Elmer C,H,N-analyzer. The course of the reaction was monitored and the purity of the compounds synthesized was checked by TLC on Silufol UV-254 plates in acetone—hexane (3 : 5); spots were visualized with iodine vapors. Melting points were determined on a Kofler microscope stage.

Anilinomethylidene derivatives of 1,3-dicarbonyl compounds 1a—c (general procedure). A mixture of a 1,3-dicarbonyl compound (0.1 mol), triethyl orthoformate (21.6 mL, 0.13 mol), and freshly distilled aniline (9.1 mL, 0.1 mol) was refluxed with vigorous stirring for 5 min and distillation of volatile products to afford a syrupy reaction mass. It was diluted with 30 mL of EtOH and refluxed for an additional 3 min. Then it was cooled with stirring to ~20 °C and diluted with water to 100 mL. After 2 h, the product was filtered off and washed with water, twice with 60% EtOH, and with hexane.

2-Anilinomethylidenecyclohexane-1,3-dione (1a). Yield 70%, m.p. 122—123 °C. Found (%): C, 72.56; H, 6.11; N, 6.50. $C_{13}H_{13}NO_2$. Calculated (%): C, 72.54; H, 6.09; N, 6.51. ^{1}H NMR, δ: 1.95 (m, 2 H, C(5)H_2); 2.45 (m, 4 H, C(4)H_2, C(6)H_2); 7.21—7.41 (m, 5 H, Ph); 8.49 (d, 1 H, CH=, ^3J = 13.3 Hz); 12.76 (d, 1 H, NH).

2-Anilinomethylidene-5,5-dimethylcyclohexane-1,3-dione (1b). Yield 89%, m.p. 137—138 °C. Found (%): C, 74.09; H, 7.07; N, 5.76. $C_{15}H_{17}NO_2$. Calculated (%): C, 74.05; H, 7.04; N, 5.76. ^{1}H NMR, δ: 1.06 (s, 6 H, 2 Me); 2.30, 2.38 (both br.s, 2 H each, $(CH_2)_2$); 7.17—7.41 (m, 5 H, Ph); 8.48 (d, 2 H, CH=, ^3J = 13.7 Hz); 12.75 (d, 1 H, NH).

5-Anilinomethylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (1c). Yield 92%, m.p. 156—157 °C. Found (%): C, 63.19; H, 5.32; N, 5.66. $C_{13}H_{13}NO_4$. Calculated (%): C, 63.15; H, 5.30; N, 5.67. ^{1}H NMR, δ: 1.70 (s, 6 H, 2 Me); 7.19—7.51 (m, 5 H, Ph); 8.58 (d, 2 H, CH=, ^3J = 14.7 Hz); 11.27 (d, 1 H, NH).

Cyanothioxohexahydroquinolinones 3a,b and dihydropyridinecarboxylic acid 4 (general procedure). Potassium hydroxide (11.2 g, 0.2 mol) was added to a vigorously stirred suspension of a 1,3-dicarbonyl compound (**1a—c**) (0.1 mol) and cyanothioacetamide (**2**) (10.01 g, 0.1 mol) in 100 mL of EtOH. After 24 h, the reaction mixture was acidified with conc. HCl to pH 5 and kept for 3 h. The precipitate that formed was filtered off and washed successively with water and EtOH.

3-Cyano-2-thioxo-1,2,5,6,7,8-hexahydroquinolin-5-one (3a). Yield 80%, m.p. >300 °C (from AcOH—DMF, 1 : 1). Found (%): C, 58.92; H, 4.01; N, 13.89. $C_{10}H_8N_2OS$. Calculated (%): C, 58.81; H, 3.95; N, 13.72.

3-Cyano-7,7-dimethyl-2-thioxo-1,2,5,6,7,8-hexahydroquinolin-5-one (3b). Yield 82%, m.p. >300 °C (from AcOH—DMF, 1 : 1). Found (%): C, 62.19; H, 5.27; N, 12.18. $C_{12}H_{12}N_2OS$. Calculated (%): C, 62.04; H, 5.21; N, 12.06.

5-Cyano-6-mercapto-2-oxo-1,2-dihydropyridine-3-carboxylic acid (4). Yield 64%, decomp. 340—345 °C (from water). Found (%): C, 43.02; H, 2.08; N, 14.41. $C_7H_4N_2O_3S$. Calculated (%): C, 42.85; H, 2.06; N, 14.28.

Tetrahydroquinolinones 6a—d (general procedure). A 10% aqueous solution of KOH (2.5 mL, 4.5 mmol) was added to a suspension of thiones **3a,b** (4.5 mmol) in 25 mL of EtOH. The reaction mixture was heated with stirring to 50 °C (until the starting reagent was dissolved) and filtered into a solution of an alkyl halide (**5a—c**) (4.5 mmol) in 10 mL of EtOH. After 12 h,

the reaction mixture was diluted with 15 mL of water, and the solid precipitate that formed was filtered off and washed with 50% EtOH.

3-Cyano-2-methylthio-5,6,7,8-tetrahydroquinolin-5-one (6a). Yield 70%, m.p. 136—138 °C (from EtOH). Found (%): C, 60.75; H, 4.66; N, 12.94. $C_{11}H_{10}N_2OS$. Calculated (%): C, 60.53; H, 4.62; N, 12.83.

3-Cyano-7,7-dimethyl-2-methylthio-5,6,7,8-tetrahydroquinolin-5-one (6b). Yield 78%, m.p. 154—156 °C (from MeOH). Found (%): C, 63.50; H, 5.82; N, 11.43. $C_{13}H_{14}N_2OS$. Calculated (%): C, 63.39; H, 5.73; N, 11.37.

2-Benzylthio-3-cyano-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-one (6c). Yield 81%, m.p. 132—134 °C (from MeOH—water, 4 : 1). Found (%): C, 70.89; H, 5.68; N, 8.82. $C_{19}H_{18}N_2OS$. Calculated (%): C, 70.78; H, 5.63; N, 8.69.

3-Cyano-2-ethylthio-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-one (6d). Yield 70%, m.p. 105—106 °C (from MeOH—water, 4 : 1). Found (%): C, 64,68; H, 6.23; N, 10.86. $C_{14}H_{16}N_2OS$. Calculated (%): C, 64.59; H, 6.19; N, 10.76.

3-Aminotetrahydrothieno[2,3-*b*]quinolin-5-ones 7a—f (general procedure). A 10% aqueous solution of KOH (2.8 mL, 5 mmol) was added to a stirred suspension of thiones **3a,b** (4.5 mmol) in 8 mL of DMF. The reaction mixture was brought to boiling and filtered into a solution of an alkyl halide **(5d—f)** (4.5 mmol) in 5 mL of DMF. The reaction mixture was stirred for 2 h, left for 24 h, and brought to boiling. Then a 10% aqueous solution of KOH (2.8 mL, 5 mmol) was added, and refluxing was continued for an additional 3 min. After 4 h, the precipitate that formed was filtered off and washed with EtOH.

3-Amino-2-carbamoyl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-5-one (7a). Yield 85%, decomp. 320 °C (from AcOH—DMF, 3 : 1). Found (%): C, 55.28; H, 4.27; N, 16.15. $C_{12}H_{11}N_3O_2S$. Calculated (%): C, 55.16; H, 4.24; N, 16.08.

3-Amino-2-(*N*-phenylcarbamoyl)-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-5-one (7b). Yield 75%, m.p. 291—292 °C (from AcOH—DMF, 4 : 1). Found (%): C, 64.19; H, 4.53; N, 12.54. $C_{18}H_{15}N_3O_2S$. Calculated (%): C, 64.08; H, 4.48; N, 12.45.

3-Amino-2-benzoyl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-5-one (7c). Yield 83%, m.p. 263—264 °C (from AcOH). Found (%): C, 67.04; H, 4.45; N, 8.66. $C_{18}H_{14}N_2O_2S$. Calculated (%): C, 67.06; H, 4.38; N, 8.69.

3-Amino-2-carbamoyl-7,7-dimethyl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-5-one (7d). Yield 78%, m.p. 278—280 °C (from AcOH—DMF, 3 : 1). Found (%): C, 58.22; H, 5.30; N, 14.61. $C_{14}H_{15}N_3O_2S$. Calculated (%): C, 58.11; H, 5.23; N, 14.52.

3-Amino-7,7-dimethyl-2-(*N*-phenylcarbamoyl)-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-5-one (7e). Yield 75%, m.p. 270—272 °C (from EtOH—Me_2CO, 1 : 1). Found (%): C, 65.82; H, 5.29; N, 11.62. $C_{20}H_{19}N_3O_2S$. Calculated (%): C, 65.73; H, 5.24; N, 11.50.

3-Amino-2-benzoyl-7,7-dimethyl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinolin-5-one (7f). Yield 80%, m.p. 232—234 °C (from AcOH). Found (%): C, 68.69; H, 5.24; N, 8.10. $C_{20}H_{18}N_2O_2S$. Calculated (%): C, 68.55; H, 5.18; N, 7.99.

6-Bromo-3-cyano-7,7-dimethyl-2-methylthio-5,6,7,8-tetrahydroquinolin-5-one (8). A suspension of quinolinone **6b** (4.19 g, 17 mmol) in 50 mL of anhydrous MeOH was heated with stirring to 50 °C, and then a solution of Br_2 (0.87 mL, 17 mmol) in 10 mL of MeOH was slowly added dropwise. The reaction mixture was stirred for an additional 30 min and diluted with water. The precipitate that formed was filtered off and washed with 50% EtOH to give compound **8** (3.32 g, 60%), m.p. 149—150 °C (from EtOH). Found (%): C, 47.95; H, 4.07; N, 8.59. $C_{13}H_{13}BrN_2OS$. Calculated (%): C, 48.01; H, 4.03; N, 8.61.

Pyridinecarboxylic acids 9a—d and 10a—c (general procedure). A 10% aqueous solution of KOH (2.97 mL, 5.3 mmol) was added to a stirred suspension of acid **4** (0.5 g, 2.6 mmol) in 10 mL of 50% aqueous ethanol. The reaction mixture was dissolved by heating and filtered into a solution of an alkyl halide **(5a—g)** (2.6 mmol) in 5 mL of EtOH. The resulting solution was refluxed for 5 min, left for 48 h, and acidified with conc. HCl to pH 5. After 3 h, the precipitate that formed was filtered off and washed with 50% EtOH.

5-Cyano-6-methylthio-2-oxo-1,2-dihydropyridine-3-carboxylic acid (9a). Yield 76%, m.p. 246—247 °C (from MeOH). Found (%): C, 45.84; H, 2.89; N, 13.36. $C_8H_6N_2O_3S$. Calculated (%): C, 45.71; H, 2.88; N, 13.33.

6-Benzylthio-5-cyano-2-oxo-1,2-dihydropyridine-3-carboxylic acid (9b). Yield 73%, m.p. 215—216 °C (from MeOH—water, 3 : 1). Found (%): C, 58.84; H, 3.53; N, 9.90. $C_{14}H_{10}N_2O_3S$. Calculated (%): C, 58.73; H, 3.52; N, 9.78.

5-Cyano-6-ethylthio-2-oxo-1,2-dihydropyridine-3-carboxylic acid (9c). Yield 70%, m.p. 229—231 °C (from MeOH—water, 3 : 1). Found (%): C, 48.33; H, 3.64; N, 12.57. $C_9H_8N_2O_3S$. Calculated (%): C, 48.21; H, 3.60; N, 12.49.

6-Allylthio-5-cyano-2-oxo-1,2-dihydropyridine-3-carboxylic acid (9d). Yield 75%, m.p. 182—185 °C (from MeOH—water, 3 : 1). Found (%): C, 50.99; H, 3.44; N, 11.89. $C_{10}H_8N_2O_3S$. Calculated (%): C, 50.84; H, 3.41; N, 11.86.

3-Amino-2-carbamoyl-6-oxo-6,7-dihydrothieno[2,3-*b*]pyridine-5-carboxylic acid (10a). Yield 66%, m.p. >300 °C (from AcOH—DMF, 1 : 1). Found (%): C, 42.78; H, 2.80; N, 16.65. $C_9H_7N_3O_4S$. Calculated (%): C, 42.69; H, 2.79; N, 16.59.

3-Amino-6-oxo-2-(*N*-phenylcarbamoyl)-6,7-dihydrothieno[2,3-*b*]pyridine-5-carboxylic acid (10b). Yield 66%, decomp. 300—303 °C (from AcOH—DMF, 1 : 1). Found (%): C, 54.83; H, 3.40; N, 12.81. $C_{15}H_{11}N_3O_4S$. Calculated (%): C, 54.71; H, 3.37; N, 12.76.

3-Amino-2-benzoyl-6-oxo-6,7-dihydrothieno[2,3-*b*]pyridine-5-carboxylic acid (10c). Yield 50%, m.p. 327—329 °C (from AcOH). Found (%): C, 57.45; H, 3.24; N, 8.99. $C_{15}H_{10}N_2O_4S$. Calculated (%): C, 57.32; H, 3.21; N, 8.91.

8-Cyano-3-iodomethyl-5-oxo-2,3,4,5-tetrahydrothiazolo[3,2-*a*]pyridine-6-carboxylic acid (11). A solution of I_2 (0.43 g, 1.7 mmol) in 30 mL of EtOH was added to a solution of compound **9d** (0.4 g, 1.7 mmol) in 20 mL of EtOH. The reaction mixture was refluxed for 5 min and then stirred at 50 °C for 6 h. After 4 days, the crystalline precipitate that formed was filtered off. The yield of acid **11** was 0.55 g (90%), m.p. 226—228 °C (from Me_2CO). Found (%): C, 33.21; H, 1.96; N, 7.76. $C_{10}H_7IN_2O_3S$. Calculated (%): C, 33.17; H, 1.95; N, 7.74.

6,6′-Dithiobis(5-cyano-2-oxo-1,2-dihydropyridine-3-carboxylic acid) (12). A 10% aqueous solution of KOH (2.97 mL, 5.3 mmol) was added to a stirred suspension of acid **4** (0.5 g, 2.6 mmol) in 10 mL of 50% EtOH. The reaction mixture was brought to boiling, filtered into a solution of 35% H_2O_2 (0.5 mL, 5.3 mmol), left at ~20 °C for 24 h, and acidified with conc. HCl

to pH 5. After 3 h, the precipitate that formed was filtered off and washed with water and EtOH. The yield of disulfide **12** was 52%, decomp. temp. 340 °C. Found (%): C, 43.13; H, 1.56; N, 14.40. $C_{14}H_6N_4O_6S_2$. Calculated (%): C, 43.08; H, 1.55; N, 14.35.

X-ray diffraction analysis of compound 11 was carried out for a single crystal 0.17×0.31×0.47 mm at ~20 °C on an Enraf-Nonius CAD4 automated four-circle diffractometer (Mo$K\alpha$ radiation, $2\theta/\omega = 1.2$, $\theta_{max} = 24°$; $0 \le h \le 6$, $-10 \le k \le 10$, $-13 \le l \le 13$). The set of 2396 collected reflections included 1818 independent ones ($R_{int} = 0.011$). The crystals of compound **11** are triclinic, $a = 5.786(4)$ Å, $b = 9.157(3)$ Å, $c = 11.801(4)$ Å, $\alpha = 104.36(3)°$, $\beta = 95.18(4)°$, $\gamma = 104.40(5)°$, $V = 578.9(5)$ Å^3, $M = 362.14$, $Z = 2$, $d_{calc} = 2.10$ g cm^{-3}, $\mu = 29.3$ cm^{-1}, $F(000) = 347$, space group $P\bar{1}$. The structure was solved by the direct method and refined by the least-squares method in the anisotropic full-matrix approximation with the CRYSTALS program package.[9] The refinement was performed for 1532 reflections with $I > 3(I)$ (the number of the refined parameters was 158, and the number of reflections per parameter was 9.7). All H atoms were located from the difference electron-density map and refined with fixed coordinates and thermal parameters (except for the H(2) atom involved in hydrogen bonding, which was refined isotropically). Refinement with the use of the Chebyshev weight scheme[10] (scheme parameters were 1.03, −0.56, 0.39, and −0.42) gave final discrepancy factors $R = 0.038$ and $R_W = 0.038$; GOF = 1.124. Tables of nonhydrogen atom coordinates have been deposited with the Cambridge Crystallographic Database.

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