3-Cyanopyridine-2(1*H*)-thiones and 3-cyano-2-(methylthio)pyridines in the synthesis of substituted 3-(aminomethyl)pyridines

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The reactions of substituted 3-cyanopyridine-2(1*H*)-thiones and 3-cyano-2-(methylthio)pyridines with lithium aluminum hydride in anhydrous diethyl ether afforded the corresponding 3-aminomethyl derivatives, which were used in the synthesis of the corresponding amides.

Key words: 3-cyanopyridine-2(1*H*)-thiones, 3-cyano-2-(methylthio)pyridines, 3-(aminomethyl)-2-(methylthio)pyridines, 6-methyl- and 4,6-dimethyl-3-(aminomethyl)pyridine-2(1*H*)-thiones, lithium aluminum hydride, reduction.

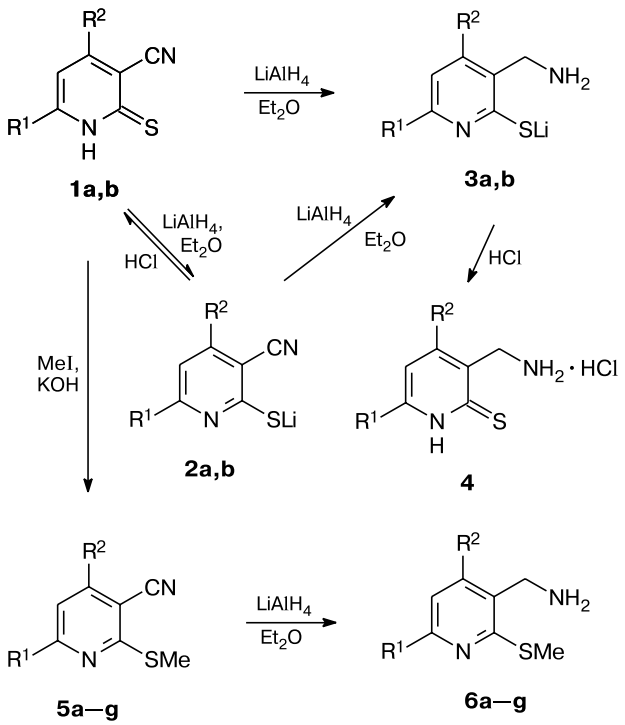
Since aminoalkyl groups are involved in many natural biologically active compounds and pharmaceuticals, the synthesis of new, including heterocyclic, compounds containing these pharmacophoric groups holds promise. From this viewpoint, compounds of the 3-cyanopyridine-2(1*H*)-thione series are of interest. These compounds attract widespread attention due to their unusual properties and broad possibilities in the synthesis of new biologically active compounds. Aminoalkyl-containing compounds of this series are unknown, although in the last 15 years considerable study was given to the chemistry of 3-cyanopyridine-2(1*H*)-thione and its derivatives, including transformations of the nitrile group.[1,2] Thus, hydrolysis of the nitrile group,[3,4] reactions with organometallic compounds,[1,4,5] and intra- and intermolecular heterocyclization involving this group[1,2,6—12] were examined. However, reduction of the nitrile group in 3-cyanopyridine-2(1*H*)-thiones has not been described, although the nitrile group in their analogs, *viz.*, in 3-cyano-2(1*H*)-pyridones, was reduced to the aldehyde group with diisobutylaluminum hydride (DIBAH).[13]

The aim of the present study was to examine the possibility of reducing the nitrile group to the aminomethyl group in substituted 3-cyanopyridine-2(1*H*)-thiones and their *S*-methyl-substituted derivatives. Products of these reactions may be of interest not only as biologically active compounds but also as synthons. We chose lithium aluminum hydride, which is widely used in the synthetic practice, as the reducing agent.

Results and Discussion

We found that reduction of 3-cyanopyridine-2(1*H*)-thione derivatives (**1a,b**) with $LiAlH_4$ in diethyl ether depended substantially on the reaction conditions. When thiones **1a,b** were added to even a substantial excess of $LiAlH_4$, the reaction was terminated at the step of forma-

Scheme 1



1—3: R^1 = Me, R^2 = H (**a**); R^1 = H, R^2 = Me (**b**)
4: R^1 = Me, R^2 = H
5, 6: $R^1 = R^2$ = Me (**a**); $R^1 = R^2$ = Ph (**b**); R^1 = Me, R^2 = H (**c**); $R^1 = Me_2C{=}CH$, R^2 = H (**d**); $R^1 = Me_2CHCH_2$, R^2 = H (**e**); $R^1 = Me_2CH$, R^2 = H (**f**); $R^1 = C_5H_{11}$, R^2 = H (**g**)

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 926—931, April, 2003.

1066-5285/03/5204-978 $25.00

tion of lithium 3-cyanopyridine-2-thiolates (**2a,b**), which were reduced to the corresponding amines **3a,b** in the repeated reactions. We succeeded in reducing thiones **1a,b** by adding $LiAlH_4$ to their suspensions in diethyl ether (Scheme 1). The highest yields (70—80%) of the amines (as lithium thiolates **3a,b**) were attained using 2 moles of $LiAlH_4$ per mole of the starting nitrile.

Amines **3** can be isolated and characterized as hydrochlorides. Thus, acidification of **3a** with hydrochloric acid and subsequent purification by recrystallization afforded 3-(aminomethyl)-6-methylpyridine-2(1*H*)thione hydrochloride (**4**). Its structure was established by IR and ^{1}H NMR spectroscopy. The IR spectrum has absorption bands in the region of 3500 cm^{-1} (NH_3^+). The ^{1}H NMR spectrum shows a singlet of the CH_2 group at δ 4.00 and a singlet of the NH fragment of the pyridine ring at δ 13.75, which is indicative of the thione structure of the compound synthesized.

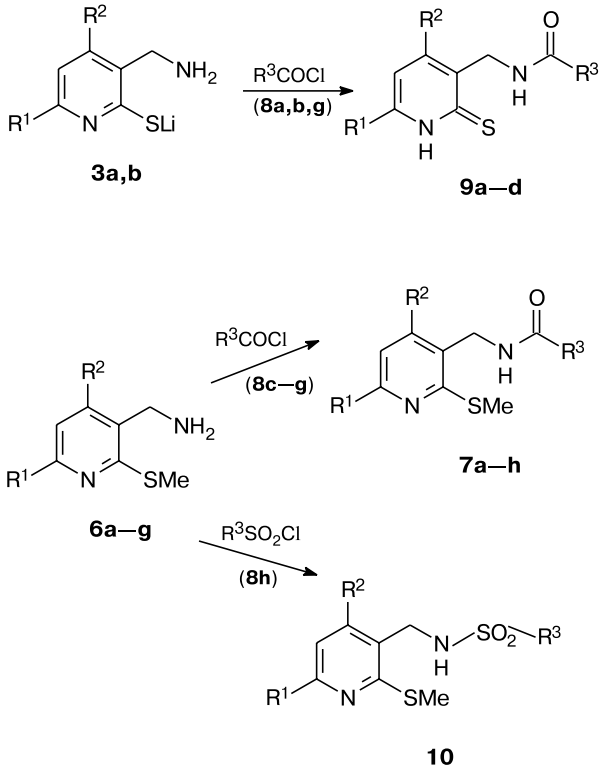
Since 3-cyanopyridine-2(1*H*)thiones are poorly soluble in diethyl ether, they were used in the reactions as readily soluble *S*-methyl derivatives **5a—g**. The latter were reduced with $LiAlH_4$ to the corresponding 3-(aminomethyl) derivatives **6a—g** in 60—80% yields (see Scheme 1).

Compounds **3a,b** and **6a—g** were prepared as pale-yellow crystalline compounds or liquids. Their structures were confirmed by IR and ^{1}H NMR spectroscopy and mass spectrometry. The IR spectra are characterized by the presence of a vibrational band of the amino group at 3300—3400 cm^{-1} and the absence of the band of the nitrile group at 2200 cm^{-1}. The ^{1}H NMR spectra have a characteristic singlet of the methylene group at δ 3.60—3.80. We failed to isolate compounds **6e—g** in the individual form. Hence, these compounds were characterized as the corresponding amides **7** and used in subsequent reactions without purification.

Lithium 3-(aminomethyl)pyridine-2-thiolates (**3a,b**) and 3-(aminomethyl)-2-(methylthio)pyridines (**6a—g**) thus synthesized were acylated with acid chlorides **8a—h** in acetonitrile in the presence of Et_3N to form amides **7a—h** and **9a—d** and sulfamide **10** (Scheme 2).

Amides **7a—h** and **9a—d** were prepared as white or pale-yellow powders. The IR spectra of these amides have characteristic absorption bands at 3250—3350 cm^{-1} (NH of the amide group) and 1620—1650 cm^{-1} (C=O). The ^{1}H NMR spectra of amides **7a—h** and **9a—d** show a doublet (in some cases, a singlet is observed due, apparently, to the fact that the signal remains unresolved) of the CH_2 group at δ 4.40—4.70 and a triplet of NH of the amide group at δ 8.00—9.50. In some cases (compounds **7g** and **9b**), the signal of the CH_2 group is observed as a quartet of doublets. In addition, the ^{1}H NMR spectra of amides **9a—d** have a broadened singlet of the NH group of the pyridine ring at δ 13.00—14.00, which indicates that these compounds have thione structures. The characteristics of compounds **3a,b**, **4**, **6a—g**, **7a—h**, **9a—d**, and **10** are given in Tables 1 and 2.

Scheme 2



7: $R^1 = R^2 = Me$, $R^3 = 3,4,5\text{-}(MeO)_3C_6H_2$ (**a**);
$R^1 = R^2 = Me$, $R^3 = 2\text{-}Me\text{-}3\text{-}NO_2C_6H_3$ (**b**);
$R^1 = R^2 = Ph$, $R^3 = 3,4,5\text{-}(MeO)_3C_6H_2$ (**c**);
$R^1 = Me_2C{=}CH$, $R^2 = H$, $R^3 = 4\text{-}ClC_6H_4$ (**d**); $R^1 = Me_2CHCH_2$,
$R^2 = H$, $R^3 = 3,4,5\text{-}(MeO)_3C_6H_2$ (**e**); $R^1 = Me$, $R^2 = H$,
$R^3 = 4\text{-}Bu^tC_6H_4$ (**f**); $R^1 = Me_2CH$, $R^2 = H$,
$R^3 = PhCH(Me)CH_2$ (**g**); $R^1 = C_5H_{11}$, $R^2 = H$, $R^3 = 4\text{-}ClC_6H_4$ (**h**);
8: $R^3 = PhOCH(Me)$ (**a**); Me (**b**); $3,4,5\text{-}(MeO)_3C_6H_2$ (**c**);
$2\text{-}Me\text{-}3\text{-}NO_2C_6H_3$ (**d**); $4\text{-}Bu^tC_6H_4$ (**e**);
$PhCH(Me)CH_2$ (**f**); $4\text{-}ClC_6H_4$ (**g, h**);
9: $R^1 = Me$, $R^2 = H$, $R^3 = 4\text{-}ClC_6H_4$ (**a**);
$R^1 = Me$, $R^2 = H$, $R^3 = PhOCH(Me)$ (**b**); $R^1 = R^2 = Me$,
$R^3 = 4\text{-}ClC_6H_4$ (**c**); $R^1 = R^2 = R^3 = Me$ (**d**);
10: $R^1 = R^2 = Ph$, $R^3 = 4\text{-}ClC_6H_4$

To summarize, the reactions of substituted 3-cyanopyridine-2(1*H*)-thiones and 2-(methylthio)-3-cyanopyridines with lithium aluminum hydride in anhydrous diethyl ether afforded 3-aminomethyl derivatives, which were used for the synthesis of the corresponding amides.

Experimental

The IR spectra were recorded on a Specord M-80 spectrophotometer in KBr pellets. The ^{1}H NMR spectra were measured on a Bruker WM-250 spectrometer (250 MHz) in DMSO-d_6 and on a Bruker DRX-500 spectrometer (500 MHz) in CCl_4—DMSO-d_6. The signal of the solvent (δ_H = 2.50) was

Table 1. Yields, melting points, and elemental analysis data for the compounds synthesized

Compound	Yield (%)	M.p./°C (solvent)	Found / Calculated (%)					Molecular formula
			C	H	Cl	N	S	
4	83	292—296 (MeOH)	43.87 44.09	5.89 5.81	18.68 18.59	14.57 14.69	16.99 16.81	$C_7H_{11}ClN_2S$
6a	59	70—72 (C_6H_{14})	59.19 59.30	7.81 7.74	—	15.24 15.37	17.76 17.59	$C_9H_{14}N_2S$
6b	45	97—107 (C_6H_{14})	74.26 74.47	5.84 5.92	—	9.02 9.14	10.88 10.46	$C_{19}H_{18}N_2S$
6c	62	71.5 (C_6H_{14})	57.32 57.11	7.11 7.19	—	16.82 16.65	18.75 19.06	$C_8H_{12}N_2S$
6d	52	70—75 (C_6H_{14})	63.28 63.42	7.79 7.74	—	13.33 13.45	15.60 15.39	$C_{11}H_{16}N_2S$
7a	72	185—190 ($EtOH/H_2O$)	60.73 60.62	6.40 6.43	—	7.36 7.44	8.66 8.52	$C_{19}H_{24}N_2O_4S$
7b	71	189—190 ($EtOH/H_2O$)	58.89 59.11	5.61 5.54	—	12.05 12.16	9.42 9.28	$C_{17}H_{19}N_3O_3S$
7c	46	213—219 ($EtOH/H_2O$)	69.49 69.58	5.70 5.64	—	5.51 5.60	6.53 6.40	$C_{29}H_{28}N_2O_4S$
7d	76	145—148 ($EtOH/H_2O$)	62.23 62.33	5.57 5.52	10.12 10.22	8.01 8.08	9.35 9.24	$C_{18}H_{19}ClN_2OS$
7e	82	122—125 ($EtOH/H_2O$)	62.17 62.35	7.07 6.98	—	6.71 6.92	8.18 7.93	$C_{21}H_{28}N_2O_4S$
7f	65	162—165 (MeCN)	69.35 69.48	7.47 7.36	—	8.39 8.53	9.92 9.76	$C_{19}H_{24}N_2OS$
7g	69	88.5—90.5 (MeOH)	70.00 70.14	7.72 7.65	—	8.06 8.18	9.49 9.36	$C_{20}H_{26}N_2OS$
7h	19	105—107 (MeOH)	62.74 62.88	6.48 6.39	9.68 9.77	7.62 7.72	8.96 8.83	$C_{19}H_{23}ClN_2OS$
9a	64	254—256 (AcOEt)	57.31 57.43	4.52 4.48	11.93 12.11	9.45 9.57	11.16 10.95	$C_{14}H_{13}ClN_2OS$
9b	55	166—168 (AcOEt)	63.34 63.55	6.06 6.00	—	9.12 9.26	10.79 10.60	$C_{16}H_{18}N_2O_2S$
9c	77	232.5—234 (MeOH)	58.59 58.72	4.98 4.93	11.41 11.56	9.02 9.13	10.58 10.45	$C_{15}H_{15}ClN_2OS$
9d	25	191—196 (AcOEt)	56.93 57.11	6.77 6.71	—	13.22 13.32	15.41 15.25	$C_{10}H_{14}N_2OS$
10	77	175.5—177 (MeCN)	62.53 62.42	4.35 4.40	7.23 7.37	5.89 5.82	13.42 13.33	$C_{25}H_{21}ClN_2O_2S_2$

used as the internal standard. The mass spectra were obtained on a Finnigan MAT INCOS-50 instrument (70 eV). Elemental analysis was carried out on a Perkin—Elmer 2400 instrument. The melting points were determined on a Kofler stage.

Lithium 3-cyanopyridine-2-thiolates (2a,b). A suspension of pyridinethione **1a,b** (10 mmol) in anhydrous Et_2O (20 mL) was added portionwise with stirring to a solution of $LiAlH_4$ (20 mmol) in anhydrous Et_2O (60 mL) for 10 min, weak refluxing being maintained. The resulting suspension was refluxed with stirring for 2 h and then water (100 mL) was added dropwise. The aqueous phase was separated and filtered. The filtrate was concentrated. Lithium salts **2a,b** were prepared in 80—90% yields.

Lithium 3-aminomethylpyridine-2-thiolates (3a,b). ***A.*** A solution of $LiAlH_4$ (10 mmol) in anhydrous Et_2O (20 mL) was added portionwise with stirring to a suspension of lithium thiolate **2a,b** (5 mmol) in anhydrous Et_2O (30 mL) for 10 min. Then the reaction mixture was worked up as described above. Lithium salts **3a,b** were prepared in 70—80% yields.

B. Salts **3a,b** were synthesized analogously from pyridinethiones **1a,b** in 70—80% yields.

3-Aminomethyl-6-methylpyridine-2(1*H*)-thione hydrochloride (4). Concentrated HCl (1 mL) was added to a solution of amine **3a** (2 mmol) in water (20 mL), water was distilled off, and the residue was recrystallized from MeOH.

Table 2. Spectroscopic characteristics of the compounds synthesized

Compound	IR, ν/cm^{-1}	MS, m/z (I (%))	^{1}H NMR, δ (J/Hz)
3a*	3417 (NH_2)	—	2.44 (s, 3 H, Me); 3.85 (m, 2 H, CH_2); 6.89 (d, 1 H, H(5), J = 7.4); 7.54 (d, 1 H, H(4), J = 7.4)
3b	3384 (NH_2)	—	—
4	3456 (NH_2), 3480 (NH_2), 3504 (NH)	—	2.40 (s, 3 H, Me); 4.00 (m, 2 H, CH_2); 6.70 (d, 1 H, H(5), J = 7.4); 7.70 (d, 1 H, H(4), J = 7.4); 8.60 (s, 3 H, NH_3^+); 13.75 (s, 1 H, NH)
6a	3408 (NH_2)	182 (18.1) $[M]^+$, 167 (100), 150 (22.3), 140 (5.3), 133 (26.6), 120 (12.8), 113 (4.8), 107 (24.5), 91 (10.6), 83 (5.3), 77 (18.1), 65 (13.3), 53 (9.6), 36 (30.9)	1.63 (br.s, 2 H, NH_2); 2.30 (s, 3 H, Me(4)); 2.37 (s, 3 H, Me(6)); 2.47 (s, 3 H, SMe); 3.72 (s, 2 H, CH_2); 6.75 (s, 1 H, H(5))
6b	3448 (NH_2)	306 (19.7) $[M]^+$, 291 (100), 274 (7.8), 257 (38.3), 240 (3.9), 215 (4.3), 189 (2.1)	1.52 (br.s, 2 H, NH_2); 2.71 (s, 3 H, SMe); 3.71 (s, 2 H, CH_2); 7.40—7.60 (m, 9 H, H(3), H(4), H(5), 4-Ph, 6-Ph); 8.10 (d, 2 H, H(2), H(6), 6-Ph, J = 7.9)
6c	3328 (NH_2)	168 (16.42) $[M]^+$, 153 (100), 135 (6.01), 126 (6.31), 119 (22.72), 105 (8.31), 93 (18.22), 77 (6.61), 65 (10.31), 44 (9.11), 39 (7.01)	2.43 (s, 3 H, Me); 2.50 (s, 3 H, SMe); 3.62 (s, 2 H, CH_2); 6.92 (d, 1 H, H(5), J = 7.4); 7.56 (d, 1 H, H(4), J = 7.4)
6d	3344 (NH_2), 1648 (C=C)	—	1.91, 2.17 (both s, 3 H each, Me); 2.50 (s, 3 H, SMe); 3.64 (s, 2 H, CH_2); 6.24 (s, 1 H, C=CH); 6.94 (d, 1 H, H(5), J = 7.4); 7.64 (d, 1 H, H(4), J = 7.4)
6f	3368 (NH_2)	—	—
6g	3304 (NH_2)	—	—
7a**	3272 (NH), 1624 (C=O)	—	2.30 (s, 3 H, Me(4)); 2.41 (s, 3 H, Me(6)); 2.50 (s, 3 H, SMe); 3.71 (s, 3 H, OMe(4)); 3.81 (s, 6 H, OMe(3), OMe(5)); 4.50 (d, 2 H, CH_2, J = 5.4); 6.81 (s, 1 H, H(5)); 7.17 (s, 2 H, H(2), H(6), Ph); 8.21 (br.s, 1 H, NH)
7b**	3272 (NH), 1632 (C=O)	345 (41.5) $[M]^+$, 330 (39), 312 (8.5), 298 (7.3), 181 (100), 164 (95.1), 147 (9.8), 136 (9.8), 118 (29.3), 106 (9.8), 90 (36.6), 77 (17.1), 65 (12.2), 53 (7.3), 40 (14.6), 34 (0.7)	2.33 (s, 3 H, Me(4)); 2.39 (s, 3 H, Me(6)); 2.40 (s, 3 H, Me(Ph(2)); 2.50 (s, 3 H, SMe); 4.48 (d, 2 H, CH_2, J = 5.4); 6.85 (s, 1 H, H(5)); 7.45 (t, 1 H, H(5), Ph, J = 8.2); 7.57 (d, 1 H, H(6), Ph, J = 7.7); 7.90 (d, 1 H, H(4), Ph, J = 8.2); 8.45 (t, 1 H, NH, J = 5.4)
7c**	3280 (NH), 1628 (C=O)	500 (17.1) $[M]^+$, 485 (2.4), 467 (1.2), 453 (18.3), 305 (75.6), 289 (43.9), 274 (6.1), 243 (4.9), 215 (6.1), 195 (100), 168 (6.1), 152 (12.2), 137 (9.8), 109 (9.3), 92 (4.9), 77 (19.5), 57 (7.3), 40 (12.7)	2.68 (s, 3 H, SMe); 3.72 (s, 3 H, OMe(4)); 3.83 (s, 6 H, OMe(3), OMe(5)); 4.37 (s, 2 H, CH_2); 7.16 (s, 2 H, H(2), H(6), COPh); 7.41—7.56 (m, 9 H, Ph, H(5)); 8.15 (d, 2 H, H(2), H(6), Ph, J = 7.9); 8.31 (br.s, 1 H, NH)
7d**	3288 (NH), 1640 (C=O)	346 (34.23) $[M]^+$, 333 (5.21), 331 (14.41), 313 (7.31), 207 (66.17), 191 (13.31), 190 (17.72), 176 (30.03), 158 (30.93), 144 (10.01), 141 (30.93), 140 (9.91), 139 (100), 131 (10.81), 130 (9.91), 117 (11.91), 113 (17.32), 111 (55.66), 91 (9.81), 77 (15.22), 75 (21.22), 51 (9.61), 41 (10.31), 39 (12.41)	1.91 (s, 3 H, Me(1)); 2.18 (s, 3 H, Me(2)); 2.55 (s, 3 H, SMe); 4.38 (d, 2 H, CH_2, J = 5.4); 6.25 (s, 1 H, C=CH); 6.95 (d, 1 H, H(5), J = 7.4); 7.44 (d, 1 H, H(4), J = 7.4); 7.56 (d, 2 H, H(3), H(5), Ph, J = 7.9); 7.92 (d, 2 H, H(2), H(6), Ph, J = 7.9); 9.04 (t, 1 H, NH, J = 5.4)

(*to be continued*)

Table 2 (*continued*)

Compound	IR, ν/cm^{-1}	MS, m/z (I (%))	^1H NMR, δ (J/Hz)
7e**	3288 (NH), 1624 (C=O)	404 (14.71) $[M]^+$, 389 (9.71), 357 (13.81), 210 (12.41), 209 (100), 196 (12.01), 195 (96.90), 193 (10.91), 152 (13.51), 151 (8.91), 150 (9.71), 122 (11.81), 81 (10.51), 77 (18.92), 43 (15.72), 41 (11.41)	0.90 (d, 6 H, 2 Me, J = 6.5); 2.10 (m, 1 H, CH); 2.54 (s, 3 H, SMe); 2.58 (d, 2 H, CHC$\underline{H}_2$, J = 4.8); 3.71 (s, 3 H, OMe(4)); 3.83 (s, 6 H, OMe(3), OMe(5)); 4.39 (d, 2 H, C$\underline{H}_2$NH, J = 5.4); 6.93 (d, 1 H, H(5), J = 7.4); 7.26 (s, 2 H, H(2), H(6), Ph); 7.42 (d, 1 H, H(4), J = 7.4); 8.84 (br.t, 1 H, NH, J = 5.4)
7f	3296 (NH), 1632 (C=O)	—	1.38 (s, 9 H, Bu^t); 2.49 (s, 3 H, Me); 2.60 (s, 3 H, SMe); 4.38 (s, 2 H, CH_2); 6.88 (d, 1 H, H(5), J = 7.4); 7.35 (d, 1 H, H(4), J = 7.4); 7.45 (d, 2 H, H(3), H(5), COAr, J = 7.9); 7.85 (d, 2 H, H(2), H(6), COAr, J = 7.9); 8.70 (br.t, 1 H, NH, J = 5.4)
7g	3280 (NH), 1640 (C=O)	342 (53.66) $[M]^+$, 327 (16.59), 309 (13.41), 295 (21.95), 237 (4.15), 195 (100), 189 (10.49), 181 (87.8), 164 (12.2), 150 (11.71), 134 (10.98), 119 (11.95), 105 (93.41), 91 (36.59), 77 (32.93), 65 (9.76), 51 (10.47), 41 (19.51)	1.25 (m, 9 H, $\underline{Me}_2$CH, PhCH$\underline{Me}$); 2.42 (m, 2 H, $COCH_2$); 2.55 (s, 3 H, SMe); 2.98 (m, 1 H, $Me_2\underline{CH}$); 3.22 (m, 1 H, $CH_2\underline{CH}$(Me)Ph); 4.10 (q.d, 2 H, C$\underline{H}_2$NH, J_1 = 15.1, J_2 = 5.4); 6.71 (d, 1 H, H(5), J = 7.4); 6.94 (d, 1 H, H(4), J = 7.4); 7.22 (m, 5 H, Ph); 7.96 (t, 1 H, NH, J = 5.4)
7h	3344 (NH), 1640 (C=O)	—	1.02 (t, 3 H, Me, J = 6.6); 1.49 (m, 4 H, CH_2(3), CH_2(4)); 1.67 (m, 2 H, CH_2(2)); 2.53 (s, 3 H, SMe); 2.81 (t, 2 H, CH_2(1), J = 6.9); 4.29 (s, 2 H, C$\underline{H}_2$NH); 6.93 (d, 1 H, H(5), J = 7.4); 7.42 (d, 1 H, H(4), J = 7.4); 7.56 (d, 2 H, H(3), H(5), Ph, J = 7.9); 7.93 (d, 2 H, H(2), H(6), Ph, J = 7.9); 9.07 (t, 1 H, NH, J = 5.4)
9a**	3288 (NH), 1632 (C=O)	292 (5.6) $[M]^+$, 153 (100), 139 (13.8), 126 (3.7), 111 (16), 92 (9.6), 65 (6.4), 41 (5.3)	2.35 (s, 3 H, Me); 4.41 (s, 2 H, CH_2); 6.60 (d, 1 H, H(5), J = 7.4); 7.25 (d, 1 H, H(4), J = 7.4); 7.57 (d, 2 H, H(3), H(5), Ph, J = 7.9); 7.93 (d, 2 H, H(2), H(6), Ph, J = 7.9); 8.91 (d, 1 H, NH(amide), J = 5.4); 13.4 (s, 1 H, NH(pyridine))
9b	3248 (NH), 1652 (C=O)	302 (20.02) $[M]^+$, 209 (12.81), 154 (11.51), 153 (100), 152 (15.32), 139 (12.41), 138 (36.54), 121 (22.02), 93 (15.92), 92 (20.32), 77 (44.94), 65 (12.41), 51 (12.11), 39 (12.01)	1.50 (d, 3 H, CH$\underline{Me}$, J = 6.8); 2.33 (s, 3 H, Me); 4.20 (quad.d, 2 H, C$\underline{H}_2$NH, J_1 = 18, J_2 = 5.8); 4.79 (q, 1 H, Me$\underline{CH}$, J = 6.8); 6.42 (d, 1 H, H(5), J = 7.4); 6.96 (m, 5 H, Ph); 7.30 (d, 1 H, H(4), J = 7.4); 8.35 (d, 1 H, NH(amide), J = 5.8); 13.39 (s, 1 H, NH(pyridine))
9c	3312 (NH), 1628 (C=O)	306 (27.66) $[M]^+$, 273 (2.13), 167 (100), 150 (13.83), 139 (12.76), 111 (8.51)	2.27, 2.29 (both s, 3 H each, Me); 4.68 (d, 2 H, $\underline{CH}_2$NH, J = 5.8); 6.52 (s, 1 H, H(5)); 7.51 (d, 2 H, H(3), H(5), Ph, J = 7.9); 7.80 (d, 2 H, H(2), H(6), Ph, J = 7.9); 8.50 (t, 1 H, NH(amide), J = 5.8); 13.35 (s, 1 H, NH(pyridine))
9d	3344 (NH), 1624 (C=O)	—	1.80 (s, 3 H, $\underline{CH}_3$CO); 2.21, 2.30 (both s, 3 H each, Me); 4.45 (d, 2 H, $\underline{CH}_2$NH, J = 5.8); 6.50 (s, 1 H, H(5)); 7.70 (t, 1 H, NH(amide), J = 5.8); 13.40 (s, 1 H, NH(pyridine))
10	3248 (NH), 1324 (S=O), 1168 (S=O)	480 (26.8) $[M]^+$, 305 (100), 289 (23.2), 257 (4.9), 227 (5.1), 202 (8.5), 189 (2.4), 175 (4.4), 152 (5.4), 128 (6.8), 111 (30), 91 (4.4), 75 (15.1), 69 (2.4), 57 (2.2), 43 (3.9)	2.70 (s, 3 H, SMe); 3.90 (s, 2 H, CH_2); 7.25—7.50 (m, 11 H, H(5), 4-Ph, 6-Ph, H(3), H(4), H(5), SO_2Ar, H(3), (5)); 7.63 (d, 2 H, H(2), H(6), SO_2Ar, J = 8.4); 7.70 (t, 1 H, NH, J = 5.4); 8.10 (d, 2 H, H (2), H(6), 6-Ph, J = 7.9)

* The ^1H NMR spectrum was recorded in D_2O.
** The ^1H NMR spectrum was recorded at 500 MHz.

3-Aminomethyl-2-(methylthio)pyridines (6a—g). A solution of 3-cyano-2-methylthiopyridine **5a—g** (5 mmol) in anhydrous Et_2O (25 mL) was added dropwise with stirring to a suspension of $LiAlH_4$ (10 mmol) in anhydrous Et_2O (50 mL) for 15 min. The resulting suspension was refluxed with stirring for 1 h and cooled. Then water (100 mL) was added dropwise. The organic phase was separated and the aqueous phase was extracted with Et_2O. The combined organic phases were dried over $MgSO_4$ and concentrated. The residue was recrystallized from hexane.

3-Acylaminomethyl-2-(methylthio)pyridines (7a—h). Triethylamine (1.5 mmol) and carboxylic acid chloride **8c—g** (1.35 mmol) were added to a suspension of amine **6a—g** (1.5 mmol) in MeCN (5 mL). The reaction mixture was heated to boiling, cooled, kept at 20 °C for 24 h, diluted with water (30 mL), and acidified with a 3% aqueous HCl solution. The precipitate that formed was filtered off, washed with water and a 10% $NaHCO_3$ solution, and recrystallized from 50% aqueous EtOH.

3-(Acylaminomethyl)pyridine-2(1*H*)-thiones (9a—d) were synthesized as described above from amines **3a,b**.

3-[(4-Chlorophenyl)sulfonylaminomethyl]-2-methylthio-4,6-diphenylpyridine (10). Triethylamine (1.5 mmol) and amide **7f** (1.35 mmol) were added to a suspension of amine **6b** (1.5 mmol) in MeCN (5 mL). The reaction mixture was heated to boiling, cooled, kept at 20 °C for 24 h, diluted with water (30 mL), and acidified with a 3% aqueous HCl solution. The precipitate that formed was filtered off, washed with water and a 10% $NaHCO_3$ solution, and recrystallized from MeCN.

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

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Received July 16, 2002;
in revised form November 11, 2002