Chemistry of Heterocyclic Compounds, Vol. 33, No. 4, 1997

ACETOACETANILIDES IN SYNTHESIS OF 4-ARYL-5-ARYLCARBAMOYL-6-METHYL-3-CYANOPYRIDINE-2(1H)-THIONES

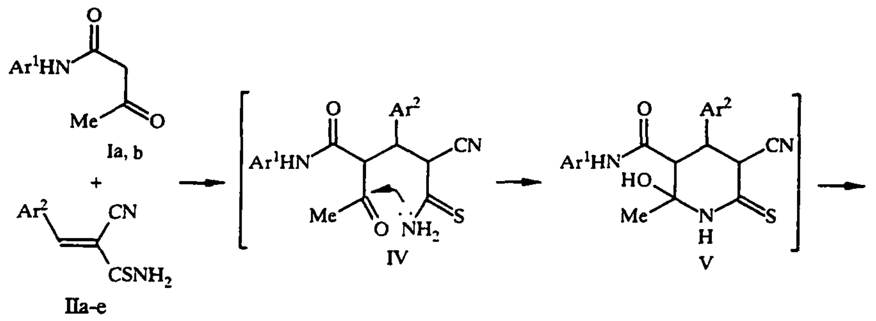
V. D. Dyachenko, S. G. Krivokolysko, and V. P. Litvinov

*The reaction of acetoacetanilides with arylmethylenecyanothioacetamides leads to 4-aryl-5-arylcarbamoyl-6-methyl-3-cyanopyridine-2(1H)-thiones, based on which we have obtained substituted 2-alkylthiopyridines and thieno[2,3-*b*]pyridines.*

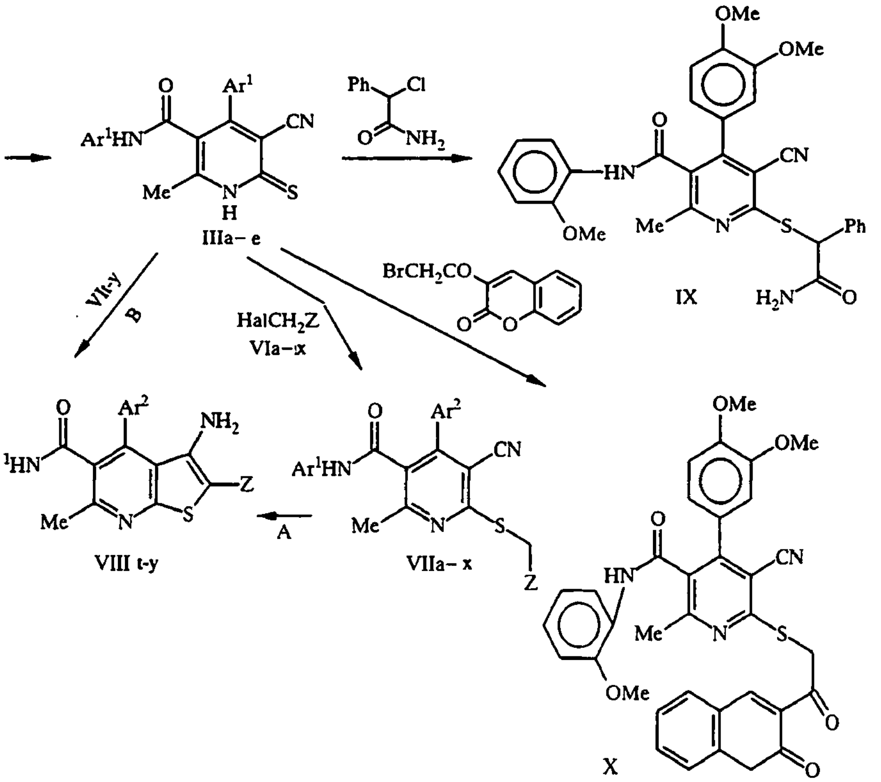
3-Cyanopyridine-2(1H)-thione and its derivatives are an important class of heterocyclic compounds of significant interest due to the diversity of their chemical reactions and the possibility of their practical application [1]. This fact, and also data on the biological activity of carbamoyl-substituted 3-cyano-3,4-dihydropyridine-2(1H)-thiones [2, 3] encouraged us to develop methods for synthesis of 3-cyanopyridine-2(1H)-thiones containing the arylcarbamoyl group.

We have shown that the reaction of acetoacetanilides (Ia, b) with arylmethylenecyanothioacetamides (IIa-e) in ethanol at 20°C in the presence of a two-fold excess of N-methylmorpholine leads to formation of 4-aryl-5-arylcarbamoyl-6-methyl-3-cyanopyridine-2(1H)-thiones (IIIa-e). Probably the reaction occurs through a step of formation of Michael adducts (IV), undergoing cyclization to substituted piperidines (V). Under the reaction conditions, the latter lose a water molecule and are dehydrogenated, forming the corresponding pyridinethiones IIIa-e. The chemical reactions support the structure of thiones IIIa-e, in particular alkylation by halides (VIa-x), phenylchloroacetamide, or bromoacetylcoumarin and intramolecular cyclization of the 2-alkylthiopyridines formed (VIIt-x) to substituted thieno[2,3-*b*]pyridines (VIIIt-y). The spectral characteristics of the synthesized pyridines (VII-X) also support their structure. Thus the IR spectra of thiones III and their derivatives VII, IX, X contain characteristic absorption bands for stretching vibrations of the conjugated nitrile group in the 2218-2232 cm^{-1} region. As a consequence of Thorpe-Ziegler cyclization [4], the signals mentioned above disappear in the spectra of thienopyridines VIII, which contain absorption bands for stretching vibrations of the amino group at 3200-3450 cm^{-1}.

The PMR spectra of the obtained compounds III, VII-X contain signals from protons of the aromatic substituents in the form of multiplets (see the experimental section and Table 2), a signal from the proton of the amide group at 10.40 ppm in the form of a singlet, signals from protons of the methyl group in the form of a singlet in the 2.40-2.60 ppm region, and also characteristic signals from protons of alkyl substituents in the corresponding regions of the spectrum (Table 2). From comparison of the PMR spectra of compounds VII and VIII, it follows that the signals from the protons of the SCH_2 group in the form of a singlet in the 3.75-4.95 ppm region disappear in the spectra of 2-alkylthiopyridines VII on going to thienopyridine VIII, whose PMR spectra now contain a signal from the protons of the amino group as a broadened singlet in the 5.62-6.74 ppm region, confirming the direction of cyclization.



T. G. Shevchenko Lugansk State Pedagogical Institute, Lugansk 348011. N. D. Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Moscow 117913. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 560-568, April, 1997. Original article submitted July 16, 1996; revision submitted December 24, 1996.



I a $Ar^1 = 2\text{-}CH_3OC_6H_4$, b $Ar^1 = Ph$; II a $Ar^2 = 3,4\text{-}(CH_3O)_2C_6H_3$, b $Ar^2 = 4\text{-}FC_6H_4$,
c $Ar^2 = 4\text{-}BrC_6H_4$, d $Ar^2 = 4\text{-}C_2H_5OC_6H_4$, e $Ar^2 = 4\text{-}CH_3OC_6H_4$; III a $Ar^1 = 2\text{-}CH_3OC_6H_4$,
$Ar^2 = 3,4\text{-}(CH_3O)_2C_6H_3$; b $Ar^1 = Ph$, $Ar^2 = 4\text{-}FC_6H_4$, c $Ar^1 = Ph$, $Ar^2 = 4\text{-}BrC_6H_4$, d $Ar^1 = Ph$,
$Ar^2 = 4\text{-}C_2H_5OC_6H_4$; e $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; VI, VII, VIII a Hal = I, Z = H, $Ar^1 = Ph$, $Ar^2 =$
$= 4\text{-}BrC_6H_4$, b Hal = Br, $Z = 2\text{-}CH_3C_6H_4$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}BrC_6H_4$; c Hal = I, $Z = CH_3$, $Ar^1 = Ph$,
$Ar^2 = 4\text{-}BrC_6H_4$, d Hal = Br, $Z = 4\text{-}BrC_6H_4CO$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}BrC_6H_4$; e Hal = Cl,
$Z = 4\text{-}BrC_6H_4NHCO$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}BrC_6H_4$; f Hal = I, Z = H, $Ar^1 = Ph$, $Ar^2 = 4\text{-}C_2H_5OC_6H_4$,
g Hal = I, $Z = CH_3$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}C_2H_5OC_6H_4$; h Hal = Cl, $Z = COOCH(CH_3)_2$,
$Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; i Hal = Cl, $Ar^1 = Ph$, $Ar^2 = Ph$, $4\text{-}CH_3OC_6H_4$; j Hal = Br,
$Z = 2\text{-}CH_3C_6H_4$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; k Hal = I, $Z = CH_3$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$,
l Hal = Br, $Z = CH{=}CH_2$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; m Hal = Br, $Z = C_2H_5$, $Ar^1 = Ph$,
$Ar^2 = 4\text{-}CH_3OC_6H_4$, n Hal = Cl, Z = PhNHCO, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$, o Hal = I, Z = H, $Ar^1 =$
$= Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$, p Hal = Br, $Z = 4\text{-}ClC_6H_4CO$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$, q Hal = Cl,
Z = CN, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; r Hal = Br, Z = PhCO, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$;
s Hal = Cl, Z = $4\text{-}BrC_6H_4NHCO$, $Ar^1 = 2\text{-}CH_3OC_6H_4$, $Ar^2 = 3,4\text{-}(CH_3O)_2C_6H_3$;
t Hal = Br, $Z = 4\text{-}BrC_6H_4CO$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; u Hal = Cl, $Z = 4\text{-}BrC_6H_4NHCO$,
$Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; v Hal = Cl, $Z = CONH_2$, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$;
w Hal = Cl, Z = COOEt, $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$; x Hal = Br, Z = PhCO, $Ar^1 = Ph$,
$Ar^2 = 4\text{-}FC_6H_4$; y Hal = Br, Z = 2-thenoyl $Ar^1 = Ph$, $Ar^2 = 4\text{-}CH_3OC_6H_4$

EXPERIMENTAL

The IR spectra of the compounds were taken on an IKS-29 spectrophotometer in Vaseline oil. The PMR spectra were recorded on a Bruker WP-100 SU (100 MHz) in DMSO-D_6 solutions with TMS as the internal standard. The course of the reaction and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 in an acetone–heptane system (3:5).

4-Aryl-5-arylcarbamoyl-6-methyl-3-cyanopyridine-2(1H)-thiones (IIIa-e). A mixture of 0.01 moles acetoacetanilide Ia, b, 0.01 moles arylmethylenecyanothioacetamide IIa-e, and 2.02 ml (0.02 moles) N-methylmorpholine in 20 ml ethanol was stirred for 4 h at 20°C. The precipitate formed was separated and then washed with ethanol and hexane.

6-Methyl-4-(3,4-dimethoxyphenyl)-5-(2-methoxyphenylcarbamoyl)-3-cyanopyridine-2(1H)-thione (IIIa). Yield 83%, mp 243-245°C (AcOH). IR spectrum: 2222 (CN), 3290 cm^{-1} (NH). PMR spectrum: 2.51 (3H, s, CH_3); 3.66, 3.74, 3.77 (3H, 3s, $(CH_3O)_3$); 7.05-7.55 (7H, m, arom.); 9.73 (1H, s, NHCO); 14.14 ppm (1H, broad s, NH). Found, %: C 63.60; H 4.91; N 9.49; S 7.20. $C_{23}H_{21}N_3O_4S$. Calculated, %: C 63.43; H 4.86; N 9.65; S 7.36.

TABLE 1. Yields, Melting Points, and Elemental Analysis of Substituted Pyridines VIIa-x, IX, X and Thieno[2,3-*b*]Pyridines VIIIt-y

Compound	mp, °C (solvent for crystallization)	Found, %				Empirical formula	Calculated, %				Yield, % (method)
		C	H	N	S		C	H	N	S	
1	2	3	4	5	6	7	8	9	10	11	12
VIIa	113...115 (ethanol)	57,30	3,51	9,64	7,48	$C_{21}H_{16}BrN_3OS$	57,54	3,68	9,59	7,31	85
VIIb	192...194 (ethanol)	63,71	4,11	8,08	5,91	$C_{28}H_{22}BrN_3OS$	63,64	4,20	7,95	6,07	69
VIIc	228...230 (ethanol)	58,50	3,87	9,40	6,89	$C_{22}H_{18}BrN_3OS$	58,41	4,01	9,29	7,09	82
VII d	231...232 (AcOH)	53,99	2,87	6,85	5,33	$C_{28}H_{19}Br_2N_3O_2S$	54,13	3,08	6,76	5,16	91
VII e	246...248 (1-butanol)	52,97	3,05	8,70	5,22	$C_{28}H_{20}Br_2N_4O_2S$	52,85	3,17	8,80	5,04	88
VII f	152...154 (methanol)	68,52	5,11	10,55	8,02	$C_{23}H_{21}N_3O_2S$	68,46	5,25	10,41	7,95	84
VII g	138...140 (methanol)	68,87	5,41	10,20	7,73	$C_{24}H_{23}N_3O_2S$	69,04	5,55	10,06	7,68	72
VII h	170...172 (ethanol)	65,78	5,44	8,69	6,65	$C_{26}H_{25}N_3O_4S$	65,67	5,30	8,84	6,74	68
VII i	172...173 (1-propanol)	72,04	5,13	8,89	7,00	$C_{28}H_{23}N_3O_2S$	72,23	4,98	9,03	6,89	77
VIIj	153...155 (ethanol)	72,71	5,39	8,64	6,50	$C_{29}H_{25}N_3O_2S$	72,63	5,25	8,76	6,69	79

TABLE 1 (continued)

Compound	mp, °C (solvent for crystallization)	Found, %				Empirical formula	Calculated, %				Yield, % (method)
		C	H	N	S		C	H	N	S	
1	2	3	4	5	6	7	8	9	10	11	12
VII.k	168...170 (ethanol)	68,30	5,14	10,61	7,88	$C_{23}H_{21}N_3O_2S$	68,46	5,25	10,41	7,95	84
VII *l*	188...189 (benzene)	69,47	4,85	10,25	7,82	$C_{24}H_{21}N_3O_2S$	69,38	5,09	10,11	7,72	71
VII m	129...131 (ethanol)	68,91	5,70	9,88	7,77	$C_{24}H_{23}N_3O_2S$	69,04	5,55	10,06	7,68	69
VII n	222...223 (1-butanol)	68,58	4,85	10,89	6,13	$C_{29}H_{24}N_4O_3S$	68,49	4,76	11,02	6,30	68
VII o	198...200 (ethanol)	68,00	5,05	10,69	8,08	$C_{22}H_{19}N_3O_2S$	67,85	4,92	10,79	8,23	80
VII p	193...195 (AcOH)	66,13	4,31	8,01	5,84	$C_{29}H_{22}ClN_3O_3S$	65,97	4,20	7,96	6,07	84
VII q	192...193 (ethanol)	66,79	4,22	13,61	7,60	$C_{23}H_{18}N_4O_2S$	66,65	4,38	13,52	7,74	69
VII r	178...180 (AcOH)	70,63	4,81	8,40	6,33	$C_{29}H_{23}N_3O_3S$	70,57	4,70	8,51	6,50	75
VII s	221...223 (1-butanol)	57,61	4,32	8,50	4,81	$C_{31}H_{27}BrN_4O_5S$	57,50	4,20	8,65	4,95	60
VII t	209...211 (AcOH)	60,71	3,70	7,42	5,80	$C_{29}H_{22}BrN_3O_3S$	60,84	3,87	7,34	5,60	85
VII u	246...248 (AcOH)	59,43	3,81	9,60	5,54	$C_{29}H_{23}BrN_4O_3S$	59,29	3,95	9,54	5,46	89
VII v	211...213 (1-butanol)	64,00	4,77	12,80	7,33	$C_{23}H_{20}N_4O_3S$	63,87	4,66	12,95	7,41	67
VII w	140...142 (1-propanol)	65,13	5,15	8,95	6,88	$C_{25}H_{23}N_3O_4S$	65,06	5,02	9,10	6,95	78
VII x	194...196 (ethanol)	69,98	4,22	8,66	6,72	$C_{28}H_{20}FN_3O_2S$	69,84	4,19	8,73	6,66	76
VIII t	124...126 (AcOH)	60,70	3,69	7,41	5,77	$C_{29}H_{22}BrN_3O_3S$	60,84	3,87	7,34	5,60	72 (A), 68 (B)

TABLE 1 (continued)

Compound	mp, °C (solvent for crystallization)	Found, %				Empirical formula	Calculated, %				Yield, % (method)
		C	H	N	S		C	H	N	S	
1	2	3	4	5	6	7	8	9	10	11	12
VIIIu	158...160* (AcOH)	59,11	3,80	9,65	5,51	$C_{29}H_{23}BrN_4O_3S$	59,29	3,95	9,54	5,46	69 (A), 70 (B)
VIIIv	276...277* (AcOH)	63,99	4,72	12,81	7,33	$C_{23}H_{20}N_4O_3S$	63,87	4,66	12,95	7,41	70 (A), 69 (B)
VIIIw	247...248 (AcOH)	65,91	4,88	9,15	6,88	$C_{25}H_{23}N_3O_4S$	65,06	5,02	9,10	6,95	77 (A), 73 (B)
VIIIx	137...139 (ethanol)	69,90	4,31	8,66	6,50	$C_{28}H_{20}FN_3O_2S$	69,84	4,19	8,73	6,66	80 (A), 74 (B)
VIIIy	289...291 (1-butanol)	65,05	4,30	8,32	12,78	$C_{27}H_{21}N_3O_3S_2$	64,91	4,24	8,41	12,84	68 (B)
IX	225...227 (1-butanol)	65,58	5,09	9,77	5,48	$C_{31}H_{28}N_4O_5S$	65,48	4,96	9,85	5,64	67
X	228...230 (AcOH)	65,50	4,22	6,81	5,28	$C_{34}H_{27}N_3O_7S$	65,69	4,38	6,76	5,16	64

---

*The materials sublime.

TABLE 2. IR and PMR Data for Compounds VIIa-x, VIIIt-y, IX, X

Compound	IR spectrum, ν, cm^{-1}		PMR spectrum, δ, ppm					
	CN, NH, NH$_2$	CO	NH, s	CH$_3$, s	Ar^1, m	Ar^2, d	SCH$_2$ s or NH$_2$, br.s	Z
1	2	3	4	5	6	7	8	9
VIIa	2225, 3220	1740	10,43	2,62	7,20	7,71, 4,40	2,69	—
VIIb	2220, 3214	1734	10,41	2,66	7,20*	7,66, 7,42	4,62	*, 2.41 s
VIIc	2222, 3230	1668	10,44	2,61	7,00...7,25	7,68, 7,48	3,32 q	1,37 t
VIId	2228, 3240	1695	10,42	2,26	7,00...7,25	7,72, 7,40	4,93	8,05 d, 7,80 d
VIIe	2225, 3362	1680, 1702	10,44	2,50	7,00...7,80*	*	4,26	10,54 s, *
VIIf	2224, 3320	1773	10,38	2,61	7,00...7,50*	*, 4,02 q, 1,30 t	2,68	—
VIIg	2223, 2230	1650	10,36	2,60	7,10...7,30	7,36, 7,00, 1,30 t, 3,29 q	4,02 q	1,32 t
VIIh	2229, 3270	1655, 1740	10,41	2,53	7,00...7,38*	*, 3,75 s	4,15	4,95 m, 1,24 d
VIIi	2225, 3250	1598	10,37	2,61	6,90...7,60*	*, 3,72 s	4,57	*
VIIj	2230, 3222	1664	10,37	2,63	6,85...7,60*	*, 3,73 s	4,60	*, 2,40 s
VIIk	2220, 3335	1680	10,39	2,60	7,15...7,35	7,45, 7,00, 3,75 s	3,32 q	1,38 t
VII*l*	2222, 3332	1700	10,40	2,60	7,10...7,30	7,39, 7,00, 3,76 s	4,03 d	5,92 m, 5,10...5,50 m
VIIm	2215, 3330	1700	10,41	2,60	7,14...7,22	7,40, 7,02, 3,76 s	3,31 t	1,75 m, 1,03 t
VIIn	2224, 3270	1665	10,36*	2,48	7,15...7,44*	7,58, 7,00, 3,73 s	4,24	*
VIIo	2230, 3344	1710	10,39	2,60	7,10...7,33	7,39, 7,01, 3,76 s	2,68	—
VIIp	2234, 3300	1684	10,40	2,27	7,15...7,33	7,45, 7,04, 3,77 s	4,94	8,15 d, 7,69 d

TABLE 2 (continued)

Compound	IR spectrum, ν, cm^{-1}		PMR spectrum, δ, ppm					
	CN, NH, NH_2	CO	NH, s	CH_3, s	Ar^1, m	Ar^2, d	SCH_2 s or NH_2, br.s	Z
1	2	3	4	5	6	7	8	9
VIIq	2218, 2244, 3210	1666	10,48	2,65	7,18...7,34	7,50, 7,02, 3,76 s	4,45	—
VII r	2220, 3272	1678, 1705	10,35	2,22	7,10...7,33	7,40, 7,00, 3,73 s	4,92	7,63...8,09 m
VII s	2219, 3270	1677	10,49	2,51	6,80...7,22*, 3,78 s	*, 3,71 c, 3,67 s	4,25	7,53 m, 9,80 s
VII t	2230, 3285	1664, 1703	10,36	2,25	7,15...7,30	7,45, 7,01, 3,76 s	4,92	8,07 d., 7,81 d
VII u	2227, 3300	1654, 1670	10,36	2,48	7,10...7,30	7,50, 7,00, 3,73 s	4,23	10,51 s., 7,55 m
VII v	2230, 3200, 3422	1650, 1683	10,42	2,57	7,25	7,38, 7,02, 3,74 s	4,03	7,69 br.s
VII w	2220, 3250	1662, 1720	10,42	2,54	7,22	7,40, 7,01, 3,76 s	4,18 m*	*, 1,25 t
VII x	2220, 3270	1650, 1680	10,39	2,27	7,00...8,13*	*	4,96	*
VIII t	3300...3460	1660	10,34	2,65	7,30	7,45, 7,07, 3,78 s	6,74	7,74 m
VIII u	3255, 3360, 3460	1650	10,35	2,63	7,25	7,40, 7,01, 3,75 s	5,85	9,63 s, 7,65 q
VIII v	3255, 3340, 3482	1657	10,35	2,62	7,05...7,55*	*, 3,74 s	5,70	*
VIII w	3300...3420	1650, 1700	10,35	2,62	7,25	7,37, 7,05, 3,76 s	5,62	1,27 t, 4,24 q
VIII x	3150, 3400	1660	10,41	2,65	7,00...7,85*	*	6,71	*
VIII y	3222, 3270, 3374	1650, 1740	10,40	2,67	7,08...7,50*	*	6,80	8,02 m, *
IX	2215, 3225	1665	9,81	2,60	7,09...7,95*, 3,80 s	*, 3,73 c, 3,65 s	5,81	*
X	2226, 3300	1664, 1740	9,78	2,40	7,07*, 3,79 s	*, 3,71 c, 3,67 s	4,90	8,79 s, 7,51...8,00 m

---

*The signals overlap

6-Methyl-5-phenylcarbamoyl-4-(4-fluorophenyl)-3-cyanopyridine-2(1H)-thione (IIIb). Yield 68%, mp 158-160°C (ethanol). IR spectrum: 2228 (CN), 3320 cm^{-1} (NH). PMR spectrum: 2.46 (3H, s, CH_3); 7.00-7.75 (9H, m, arom.); 10.21 ppm (1H, s, NHCO). Found, %: C 65.89; H 3.77; N 11.60; S 8.93. $C_{20}H_{14}FN_3OS$. Calculated, %: C 66.10; H 3.88; N 11.56; S 8.82.

4-(4-Bromophenyl)-6-methyl-5-phenylcarbamoyl-3-cyanopyridine-2(1H)-thione (IIIc). Yield 70%, mp 269-271°C (AcOH). IR spectrum: 2224 (CN), 3330 cm^{-1} (NH). PMR spectrum: 2.45 (3H, s, CH_3): 7.00-7.25 (5H, m, Ph); 7.35, 7.66 (4H, 2d, 4-BrC_6H_4); 10.30 (1H, s, NHCO); 14.38 ppm (1H, broad s, NH). Found, %: C 56.54; H 3.22; N 9.81; S 7.64. $C_{20}H_{14}BrN_3OS$. Calculated, %: C 56.61; H 3.33; N 9.90; S 7.56.

6-Methyl-5-phenylcarbamoyl-4-(4-ethoxyphenyl)-3-cyanopyridine-2(1H)-thione (IIId). Yield 74%, mp 242-244°C (ethanol). IR spectrum: 2230 (CN), 3375 cm^{-1} (NH). PMR spectrum: 1.29 (3H, t, CH_3); 2.45 (3H, s, $C_{(6)}-CH_3$); 4.01 (2H, q, CH_2); 7.10-7.25 (5H, m, Ph); 6.97, 7.50 (4H, 2d, $C_{(4)}-Ar$ (arom.)); 10.26 (1H, s, NHCO); 14.30 ppm (1H, s, NH). Found, %: C 67.92; H 4.84; N 10.89; S 8.06. $C_{22}H_{19}N_3O_2S$. Calculated, %: C 67.85; H 4.92; N 10.79; S 8.23.

6-Methyl-4-(4-methoxyphenyl)-5-phenylcarbamoyl-3-cyanopyridine-2(1H)-thione (IIIe). Yield 81%, mp 263-265°C (ethanol). IR spectrum: 2223 (CN), 3384 cm^{-1} (NH). PMR spectrum: 2.44 (3H, s, CH_3); 3.74 (3H, s, CH_3O); 7.10-7.25 (5H, m, Ph); 6.98, 7.50 (4H, 2d, $C_{(4)}-Ar$ (arom.)); 10.21 (1H, s, NHCO); 14.18 ppm (1H, broad s, NH). Found, %: C 67.24; H 4.37; N 10.95; s 8.63. $C_{21}H_{17}N_3O_2S$. Calculated, %: C 67.18; H 4.56; N 11.19; S 8.54.

4-Aryl-5-arylcarbamoyl-6-methyl-2-*Z*-methylthio-3-cyanopyridines (VIIa-x, IX, X). A 5.6 ml portion (0.01 moles) of a 10% KOH aqueous solution was added with stirring to a suspension of 0.01 moles of the corresponding pyridinethione IIIa-e in 10 ml DMF. After 1 min, 0.01 moles alkylhalide VIa-x or phenylchloroacetamide or bromoacetylcoumarin respectively was added. The reaction mixture was stirred for 2 h, then 10 ml water was added. The precipitate formed was separated and washed with water, ethanol, and hexane. Compounds VIIa-x, IX, X were obtained (Tables 1 and 2).

3-Amino-4-aryl-5-arylcarbamoyl-6-methyl-2-*Z*-thieno[2,3-*b*]pyridines (VIIIt-y). A. A 5.6 ml portion (0.01 moles) of a 10% KOH aqueous solution was added with stirring to a solution of 0.01 moles of the corresponding pyridine VIIt-y in 15 ml DMF. The reaction mixture was stirred for 4 h, then 15 ml water was added. The precipitate formed was separated and washed with water, ethanol, and hexane. Compounds VIIIt-y were obtained (Tables 1 and 2).

B. A 5.6 ml portion of a 10% KOH aqueous solution was added with stirring to a suspension of 0.01 moles of the corresponding thione IIIb, c, e in 15 ml DMF. After 1 min, 0.01 moles alkylhalide VIt-y was added to the reaction mixture. After stirring for 30 min at 20°C, 5.6 ml of a 10% KOH aqueous solution was again added to the reaction mass and it was stirred for 4 h longer. Water (15 ml) was added to the reaction mixture. The precipitate formed was separated and then washed with water, ethanol, and hexane. Compounds VIIIt-y were obtained (Tables 1 and 2).

REFERENCES

1. V. P. Litvinov, L. A. Rodinovskaya, Yu. A. Sharanin, A. M. Shestopalov, and A. Senning, Sulfur Reports, **13**, 1 (1992).
2. A. A. Krauze, A. G. Odynets, A. A. Verreva, S. K. Germane, A. N. Kozhukov, and G. Ya. Dubur, Khim.-farm. Zh., **25**, 40 (1991).
3. V. V. Kastron, R. O. Vitolinya, and G. Ya. Dubur, Khim.-farm. Zh., No. 6, 14 (1990).
4. F. S. Babichev, Yu. A. Sharanin, V. P. Litvinov, V. K. Promonenkov, and Yu. M. Volovenko, Intramolecular Reaction of Nitrile with C–H, O–H, and S–H Groups [in Russian], Naukova Dumka (1985).