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SYNTHESIS AND SOME REACTIONS OF 3-CYANOPYRIDINE-2-THIONES

A. A. Krauze, Z. A. Bomika,
A. M. Shestopalov, L. A. Rodinovskaya,
Yu. É. Pelcher, G. Ya. Dubur,
Yu. A. Sharanin, and V. K. Promonenkov

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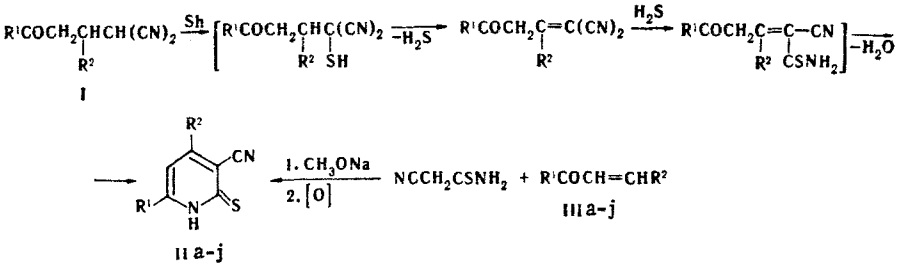
New methods for the synthesis of 3-cyanopyridine-2-thiones by the reaction of δ-keto nitroles with sulfur and by condensation of chalcones or benzylideneacetone with cyanothioacetamide are given. The compounds obtained were used in various reactions for the preparation of alkylated products, disulfides, and condensed heterocycles, viz., thieno[2,3-b]pyridines and pyrido[2',3':2,3]thieno[4,5-d]-pyrimidines.

3-Cyanopyridine-2-thiones are of interest as physiologically active substances [1, 2], as well as intermediates in the synthesis of new condensed heterocyclic systems [3] that are difficult to obtain by other methods. Up until now, the principal methods for their preparation have been the reaction of 2-chloro-3-cyanopyridines with alkali metal sulfides or thiourea [4, 5] and the condensation of β-dicarbonyl compounds with cyanothioacetamide [6].

We have developed two new methods for the preparation of 3-cyanopyridine-2-thione derivatives (II). The first method consists in the thiolation of δ-keto nitriles I, which are readily formed in the reaction of chalcones with malononitrile. In contrast to the data in [7], the use of organic bases such as morpholine gives better results in the synthesis of nitriles I. In the second method 3-cyanopyridine-2-thiones (II) are formed by the reaction of chalcones IIIa-c,g-i or benzylideneacetone (IIIj) with cyanothioacetamide in the presence of sodium methoxide. The reactions under consideration supplement one another satisfactorily and can be recommended for preparative purposes.



I, II, IIIa $R^1=R^2=C_6H_5$; b $R^1=C_6H_5$, $R^2=p$-ClC_6H_4; c $R^1=C_6H_5$, $R^2=p$-$CH_3OC_6H_4$; I, IId $R^1=p$-$CH_3OC_6H_4$, $R^2=C_6H_5$; e $R^1=p$-$CH_3C_6H_4$, $R^2=C_6H_5$; f $R^1=p$-FC_6H_4, $R^2=C_6H_5$; II, III g $R^1=C_6H_5$, $R^2=p$-$NO_2C_6H_4$; h $R^1=C_6H_5$, $R^2=p$-$(CH_3)_2NC_6H_4$; i $R^1=C_6H_5$, $R^2=o$-$F_2CHOC_6H_4$; j $R^1=CH_3$, $R^2=C_6H_5$

To confirm the structure of the isolated pyridine-2-thiones II we obtained 3-cyano-4,6-

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. T. G. Shevchenko Voroshilovgrad State Pedagogical Institute, Voroshilovgrad 348011. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 377-382, March, 1981. Original article submitted July 17, 1980.

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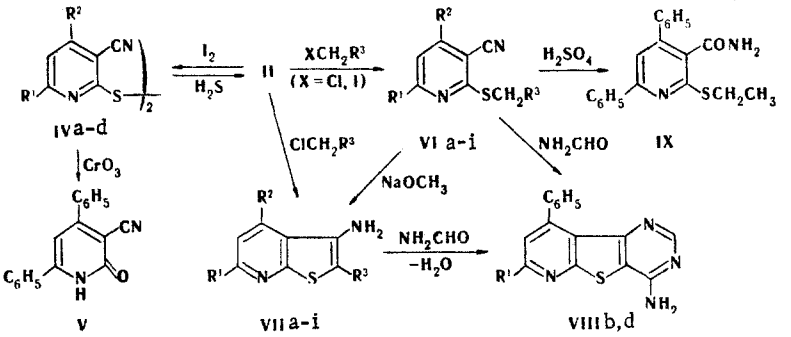
diphenylpyridine-2-thione (IIa) by alternative synthesis from 2-bromo-4,6-diphenyl-3-cyanopyridine and thiourea [5], as well as from dibenzoylmethane and cyanothioacetamide [6].

3-Cyanopyridine-2-thiones II are orange-yellow stable (in the crystalline state) substances, the UV spectra of which contain a characteristic long-wave absorption maximum at 402-423 nm. The PMR spectra of pyridine-2-thiones IIa-i contain, in addition to signals of aryl protons in the 4 and 6 positions, signals of 5-H protons at 6.96-7.12 ppm and protons of an NH group at 13.6-14.3 ppm. In the case of 3-cyano-4-phenyl-6-methylpyridine-2-thione (IIj) the signal of the 5-H proton is shifted to the strong-field side to 6.4 ppm. A characteristic absorption band of a CN group is observed in the IR spectra of II at 2215-2236 cm^{-1}.

In solutions under the influence of air oxygen pyridine-2-thiones undergo further oxidation to the corresponding 2,2'-bis(3-cyano-4,6-diarylpyridyl) disulfides (IV). Disulfides IV were obtained preparatively by oxidation of thiones II with a 10% solution of iodine in ethanol. Reconversion to pyridine-2-thiones II is readily accomplished by the action of hydrogen sulfide on disulfides IV.



IV a $R^1=R^2=C_6H_5$; b $R^1=C_6H_5$, $R^2=p$-ClC_6H_4; c $R^1=C_6H_5$, $R^2=o$-$F_2CHOC_6H_4$; d $R^1=CH_3$, $R^2=C_6H_5$; VI, VII, VIII a $R^1=R^2=C_6H_5$, $R^3=CN$; b $R^1=p$-FC_6H_4, $R^2=C_6H_5$, $R^3=CN$; c $R^1=p$-$CH_3OC_6H_4$, $R^2=C_6H_5$, $R^3=CN$; d $R^1=p$-$CH_3C_6H_4$, $R^2=C_6H_5$, $R^3=CN$; e $R^1=R^2=C_6H_5$; $R^3=COOCH_3$; f $R^1=R^2=C_6H_5$, $R^3=CH_3$; g $R^1=C_6H_5$, $R^2=p$-$(CH_3)_2NC_6H_4$, $R^3=CH_3$; h $R^1=C_6H_5$, $R^2=o$-$F_2CHOC_6H_4$, $R^3=CH_3$; i $R^1=R^3=CH_3$, $R^2=C_6H_5$

Molecular ions (M^+) of the corresponding dimers are recorded in the mass spectra of disulfides IV, while signals of protons of the NH group are absent in the PMR spectra. The corresponding 2-pyridone V is formed by further oxidation of disulfide IVa with chromic anhydride [8].

Pyridine-2-thiones are readily alkylated in the presence of bases at the sulfur atom to give alkylmercaptopyridines VI. Further cyclization of alkylthio derivatives VI via the Thorpe reaction to 3-amino-2-cyano(or 2-carbomethoxy)-4,6-diarylthieno[2,3-b]pyridines (VII) is observed in the case of electron-acceptor substituents in the thioalkyl group (R^3 = CN, $COOCH_3$) under the influence of alkali metal alkoxides or by thermal action. It should be noted that intermediate noncyclic alkyl derivatives of the VIa-e type have not yet been isolated in such reactions [3, 5, 9].

Two absorption bands of stretching vibrations of cyano groups, viz., an intense band of a conjugated nitrile group in the 3 position of the pyridine ring at 2210-2220 cm^{-1}, and a weak band of an unconjugated nitrile group at 2245-2250 cm^{-1}, are observed in the IR spectra of alkylthio derivatives VIa-d. The IR spectrum of VIe contains, inaaddition to a band of a nitrile group (2219 cm^{-1}), a characteristic band of an ester group at 1735 cm^{-1}. The absorption band of an unconjugated nitrile group vanishes in the IR spectra during the cyclization of VIa-d, and a number of bands of stretching vibrations of an amino group at 3220-3460 cm^{-1} and of deformation vibrations at 1630-1650 cm^{-1}, which confirm the thieno[2,3-b]pyridine structure of VII, appear.

Compounds VIIb,d were also characterized by conversion to 8-amino-2,4-diarylpyrido-[2',3':2,3]thieno[4,5-d]pyrimidines (VIIIb,d) by heating with formamide, while alkylthio derivatives VIf were characterized by hydrolysis of the nitrile group to the corresponding 2-ethylmercapto-3-carbamoyl-4,6-diphenylpyridine (IX). Pyridothienopyrimidines VIII are also formed by heating VIb,d with formamide; thienopyridines VIIb,d in all likelihood act as intermediates in this case.

TABLE 1. 1,1-Dicyano-2-aryl-3-aroylpropanes (I)

Compound	mp, °C	IR spectrum, cm^{-1}		Found, %			Empirical formula	Calc., %			Yield, %
		CO	CN	C	H	N		C	H	N	
Ia	125—126*	1680	2258								81
Ib	115—116	1680	2258	69,6	4,3	9,1	$C_{18}H_{13}ClN_2O$	69,8	4,6	9,0	77
Ic	117	1675	2255	75,1	5,3	9,2	$C_{19}H_{16}N_2O_2$	75,0	5,3	9,2	72
Id	123—124	1676	2256	74,8	5,1	9,3	$C_{19}H_{16}N_2O_2$	75,0	5,3	9,2	74
Ie	132—133	1674	2260	78,9	5,4	10,0	$C_{19}H_{16}N_2O$	79,1	5,6	9,7	70
If	103—104	1682	2257	73,9	4,5	9,6	$C_{18}H_{13}FN_2O$	74,0	4,5	9,6	72

*According to the data in [7], this compound has mp 126-127°C.

TABLE 2. 3-Cyano-4,6-Disubstituted Pyridine-2-thiones (II) and 2,2'-Bis(3-cyano-4,6-disubstituted pyridyl) Disulfides (IV)

Compound	Meth. of prep.	mp, °C	R_f	IR spec., cm^{-1} (CN)	UV spectrum (in ethanol), λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	PMR spectrum δ, ppm		Found, %				Empirical formula	Calc., %				Yield, %
						5-H	NH	C	H	N	S		C	H	N	S	
IIa	A	227—229	0,65	2230	245 (18,0), 288 (29,2), 315 i (22,4), 418 (5,1)	7,07	14,20	74,6	4,0	10,0	10,9	$C_{18}H_{12}N_2S$	75,0	4,2	9,9	11,1	75
	B	228—230	0,65					74,7	4,4	9,8	11,1						73
	C	228—230	0,65					74,6	3,9	9,7	10,9						80
	D	228—229	0,65					74,7	4,4	9,7	11,2						82
IIb	A	232—234	0,60	2229	245 (14,6), 305 (26,6), 418 (4,8)	7,04	14,30	67,3	3,6	8,6	9,8	$C_{18}H_{11}ClN_2S$	67,2	3,4	8,7	9,9	80
	B	225—227	0,60					67,5	3,6	8,4	9,6						43
IIc	A	223—225	0,60	2223	282 (18), 320 (28,8), 416 (4,8)	7,06	13,24	72,0	4,1	9,1	10,1	$C_{19}H_{14}N_2OS$	71,7	4,4	8,8	10,1	72
	B	226—228	0,60					71,2	4,3	8,7	10,5						72
IId	A	223—225	0,62	2220	255 (13,2), 316 (33,6), 418 (6,9)	6,96	14,00	71,7	4,6	9,0	10,2	$C_{19}H_{14}N_2OS$	71,7	4,4	8,8	10,1	70
IIe	A	190—192	0,64	2228	245 (11,3), 305 (21,2), 420 (3,9)	7,04	14,10	75,1	4,2	9,1	10,2	$C_{19}H_{14}N_2S$	75,5	4,7	9,3	10,6	89
IIf	A	200—202	0,61	2215	244 (10,6), 290 (16,6), 315 (13,2), 416 (2,8)	7,04	14,20	70,6	3,3	9,4	10,1	$C_{18}H_{11}FN_2S$	70,6	3,6	9,1	10,5	82
IIg	B	226—228	0,66	2233	246 i (11,6), 292 (21,6), 421 (3,3)	7,12	14,10	64,7	3,2	13,1	9,0	$C_{18}H_{11}N_3O_2S$	64,8	3,3	12,6	9,6	36
IIh	B	260—262	0,64	2225	272 (16,0), 321 (18,8), 413 (19,2)	6,96	13,71	72,1	5,6	13,0	10,1	$C_{20}H_{17}N_3S$	72,5	5,2	12,7	9,7	34
IIi	B	228—230	0,66	2236	241 (11,8), 282 (16,8), 317 (15,6), 417 (4,0)	7,09	13,60	64,1	3,5	8,3	9,1	$C_{19}H_{12}F_2N_2OS$	64,4	3,4	7,9	9,1	37
IIj	B	274—276	0,35	2231	226 i (10,0), 280 i (11,6), 312 (18,4), 406 (3,2)	6,40	13,93	68,8	4,5	11,8	14,0	$C_{13}H_{10}N_2S$	69,0	4,5	12,4	14,2	53
IVa		243—244	0,88	2235	275 (52,0), 336 (17,4)	8,02	—	75,8	4,1	9,3	11,5	$C_{36}H_{22}N_4S_2$	75,3	3,9	9,7	11,2	56
IVb		217—219	0,85	2230	274 (62,4), 332 (22,6)	8,05	—	66,6	3,0	8,2	10,6	$C_{36}H_{20}Cl_2N_4S_2$	67,1	3,1	8,7	10,0	80
IVc		207—209	0,90	2231	227 (32,4), 273 (47,2), 331 (22,4)	8,08	—	63,9	3,3	7,6	9,1	$C_{38}H_{22}F_4N_4O_2S_2$	64,6	3,1	7,9	9,1	77
IVd		188—190	0,84	2228	220 i (32,0), 260 (38,8), 320 i (8,2)	7,22	—	68,4	4,1	11,7	13,7	$C_{26}H_{18}N_4S_2$	69,3	4,0	12,4	14,2	84

EXPERIMENTAL

The IR spectra were recorded with Perkin—Elmer (KBr pellets) and UR-20 (suspensions in mineral oil and hexachlorobutadiene) spectrometers. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra were recorded with a Perkin-Elmer R-12A spectrometer (60 MHz) with tetramethylsilane as the internal standard. The course of the reaction and the individuality of the substances were monitored by means of thin-layer chromatography (TLC) on Silufol UV-254 plates in a chloroform—acetone—hexane system (2:1:1).

1,1-Dicyano-2-aryl-3-aroylpropanes (I). A 0.1-ml sample of morpholine was added with vigorous stirring to a solution of 10 mmole of the corresponding chalcone and 0.7 g (11 mmole) of malononitrile in 25-30 ml of ethanol, the mixture was maintained at 20°C for 1-3 h, and the precipitate was removed by filtration. The I were recrystallized from ethanol. Data on I are presented in Table 1.

3-Cyano-4,6-diphenylpyridine-2-thione (IIa). A) A mixture of 2.74 (10 mmole) of 1,1-dicyano-2-phenyl-3-benzoylpropane (Ia), 0.7 g (10.5 mmole) of powdered sulfur, and 1.5 ml of

morpholine in 35 ml of isopropyl alcohol (or ethanol) was heated with stirring for 2 h. The mixture was then acidified with 10% hydrochloric acid, and the precipitate was removed by filtration and washed with water and alcohol to give 2.16 g of thione IIa, which was recrystallized from nitromethane.

B) A 2.08-g (10 mmole) sample of chalcone IIIa and 1.0 g (10 mmole) of cyanothioacetamide were dissolved in 15 ml of an 8.5% solution of sodium methoxide, and the solution was heated on a water bath for 1.5 h. The precipitate was recrystallized from acetic acid to give 2.1 g of IIa.

C) A solution of 3.35 g (10 mmole) of 2-bromo-3-cyano-4,6-diphenylpyridine and 2.28 g (30 mmole) of thiourea in 30 ml of DMF was heated on an air bath for 4 h, after which it was cooled and acidified. The precipitate was recrystallized from nitromethane to give 2.3 g of IIa.

D) A 2-ml sample of trimethylamine was added to a solution of 2.24 g (10 mmole) of dibenzoylmethane and 1.0 g (10 mmole) of cyanothioacetamide in 20 ml of absolute alcohol, and the mixture was heated on a water bath for 2 h. It was then cooled and acidified with acetic acid, and the precipitate was recrystallized from acetic acid to give 2.37 g of IIa.

Compounds IIb-j were obtained in the same way as IIa. Data on 3-cyanopyridine-2-thiones II are presented in Table 2. In the preparation of thiones II by method A the reaction time was monitored chromatographically on Silufol in an acetone–hexane system (3:5). A total of 1-2 h was usually required for the completion of the reaction.

o-Difluoromethoxybenzalacetophenone (IIIi). A suspension of 2.4 g (20 mmole) of acetophenone and 3.44 g (20 mmole) of o-difluoromethoxybenzaldehyde [10] in 6 ml of ethanol and 10 ml of 3 N KOH solution was stirred vigorously at 20°C for 5 h, after which it was maintained at 0°C for 20 h, and the precipitate was separated. The yield of IIIi, with mp 35-37°C (from petroleum ether) and R_f 0.8, was 3.65 g (67%). IR spectrum: 1667 cm^{-1} (C=O). PMR spectrum (in d_6-DMSO): 7.18-8.24 (9H, m, C_6H_5 and C_6H_4), 8.18 (1H, d, J = 2.2 Hz, β-CH), 7.43 (1H, d, J = 2.2 Hz, α-CH), and 7.26 ppm (1H, t, J = 74 Hz, CHF_2). Found: C 70.6; H 4.7%. $C_{16}H_{12}F_2O_2$. Calculated: C 70.1; H 4.4%.

2,2'-Bis(3-cyano-4,6-diphenylpyridyl) Disulfide (IVa). A 10-ml sample of a 10% solution of iodine in ethanol was added with vigorous stirring to a solution of 1.15 g (4 mmole) of pyridine-2-thione IIa in 15 ml of 1 N NaOH solution, and the resulting precipitate was washed with ethanol and crystallized from chloroform to give 1.28 g of IVa with M^+ 574 (by mass spectroscopy).

Compounds IVb-e were similarly obtained. Data on disulfides IV are presented in Table 2.

3-Cyano-4,6-diphenyl-2-pyridone (V). A solution of 0.3 g (3.0 mmole) of chromium trioxide in 5 ml of water was added to a suspension of 0.29 g (0.5 mmole) of disulfide IVa in 40 ml of acetic acid, and the mixture was refluxed for 2.5 h. It was then cooled and diluted with water, and the precipitate was separated to give 0.12 g (43%) of pyridone V with mp 312-314°C; no melting-point depression was observed for a mixture of this product with a genuine sample [8].

3-Cyano-4,6-diaryl-2-alkylmercaptopyridines (VIa-e). A 10-ml sample of a 10% solution of potassium hydroxide was added to a suspension of 10 mmole of pyridine-2-thione II in 30 ml of DMF, after which a solution of 10 mmole of chloroacetonitrile or chloromethyl acetate in 5 ml of DMF was added dropwise. After 30 min, the reaction mixture was diluted with water, and the precipitate was removed by filtration. The temperature of the reaction mixture during the experiment should be maintained at no higher than 15-20°C. Recrystallization from benzene gave VIb,d,e. Compounds VIa,c were purified by chromatography on silica gel by elution with acetone–hexane (3:5). Evaporation of the second fraction and recrystallization of the residue from benzene gave VIa,c.

Data on VIa-e are presented in Table 3.

3-Cyano-4-aryl-6-phenyl(methyl)-2-ethylmercaptopyridines (VIf-i). A 5-mmole sample of the corresponding pyridine-2-thione II was dissolved in 10 ml of an 8.5% solution of sodium methoxide, 30 mmole of ethyl iodide was added, and the mixture was refluxed on a water bath for 1 h. The solvent was evaporated, and the precipitate was removed by filtration, washed with water, and recrystallized from ethanol.

TABLE 3. 3-Cyano-4,6-disubstituted 2-Alkylmercaptopyridines (VI) and 3-Amino-2-cyano-(2-carbomethoxy)4,6-diarylthioeno-[2,3-b]pyridines (VII)

Compound	mp, °C	IR spectrum, cm^{-1}	Found, %				Empirical formula	Calc., %				Yield, %
			C	H	N	S		C	H	N	S	
VIa	228—229	2210, 2243	72,9	4,1	13,4	10,0	$C_{20}H_{13}N_3S$	73,4	4,0	12,8	9,8	30
VIb	231—232	2212, 2243	69,5	3,5	11,9	9,0	$C_{20}H_{12}FN_3S$	69,6	3,5	12,2	9,3	61
VIc	202	2213, 2245	70,7	4,4	11,7	8,7	$C_{21}H_{15}N_3OS$	70,6	4,2	11,8	9,0	42
VId	221—222	2218, 2248	73,8	4,3	12,2	8,2	$C_{21}H_{15}N_3S$	73,9	4,4	12,3	9,4	67
VIe	186—187	2219, 1735	69,9	4,4	7,6	8,6	$C_{21}H_{16}N_2O_2S$	70,0	4,5	7,8	8,9	64
VIf	104—106	2223	76,1	5,4	9,0	10,2	$C_{20}H_{16}N_2S$	75,9	5,1	8,9	10,1	73
VIg	161—163	2222	72,3	5,9	11,4	8,3	$C_{22}H_{21}N_3S$	73,5	5,9	11,7	8,9	84
VIh	95—97	2229	66,2	4,2	7,7	8,2	$C_{21}H_{16}F_2N_2OS$	66,0	4,2	7,3	8,4	57
VIi	88—89	2224	71,0	5,7	10,7	11,9	$C_{15}H_{14}N_2S$	70,8	5,6	11,0	12,6	71
VIIa	237—239*	1630, 2211, 3222, 3327, 3460										65
VIIb	239—240	1630, 2200, 3210, 3313, 3360	69,5	3,5	12,1	9,2	$C_{20}H_{12}FN_3S$	69,6	3,5	11,8	9,0	60
VIIc	212—213	1630, 3220, 3330, 3462	70,9	4,3	12,0	9,0	$C_{21}H_{15}N_3OS$	70,6	4,2	11,8	9,0	55
VIId	251—252	1630, 2200, 3220, 3322, 3460	73,2	4,3	12,2	9,3	$C_{21}H_{15}N_3S$	73,9	4,4	12,3	9,4	53
VIIe	165—166	1650 sh 1678, 3330, 3468	69,8	4,2	7,7	8,7	$C_{21}H_{16}N_2O_2S$	70,0	4,5	7,8	8,9	46

*According to the data in [5], this compound has mp 236-237°C.

Data on VIf-i are presented in Table 3.

2-Cyano-3-amino-4,6-diphenylthieno[2,3-b]pyridines (VII). A) Compound VIIa was obtained by the method used for VIa-e with collection of the first fraction after chromatography on silica gel. Evaporation of this fraction and recrystallization of the residue from ethyl acetate gave thienopyridine VIIa with mp 237-239°C.

Compounds VIIb-e were similarly obtained.

B) A 5-ml sample of a 10% solution of sodium methoxide was added to a suspension of 1.6 g (5 mmole) of cyanomethylmercaptopyridine VIa in 20 ml of ethanol, and the mixture was heated on a water bath for 30 min. The precipitate was removed by filtration and recrystallized from ethyl acetate to give 1.0 g (60%) of VIIa with mp 237-239°C.

Thienopyridine VIIc was similarly obtained.

Data on 3-aminothieno[2,3-b]pyridines VII are presented in Table 3.

8-Amino-4-phenyl-2-(4-fluorophenyl)pyrido[2',3':2,3]thieno[4,5-d]pyrimidine (VIIIa). A 0.5-g (1.45 mmole) sample of thienopyridine VIIb or the same amount of 2-cyanomethylmercaptopyridine VIb in 5 ml of formamide was heated for 15 min in a flask equipped with an air condenser. The precipitate was removed by filtration and recrystallized from nitromethane to give 0.22 g (40%) of VIIIa with mp 282-283°C. IR spectrum: 3440, 3300, and 1650 cm^{-1} (NH_2). Found: C 67.7; H 3.4; N 15.0; S. 8.6%. $C_{21}H_{13}FN_4S$. Calculated: C 67.7; H 3.5; N 15.0; S 8.8%.

8-Amino-2-(4-tolyl)-4-phenylpyrido[2',3':2,3]thieno[4,5-d]pyrimidine (VIIIb). This compound, with mp 268-270°C (from nitromethane), was obtained in 56% yield by the method used to prepare VIIIa. IR spectrum: 3370, 3320, 3200, and 1643 cm^{-1} (NH_2). Found: C 71.3; H 4.6; N 15.6; S. 8.9%. $C_{22}H_{16}N_4S$. Calculated: C 71.7; H 4.4; N 15.2; S 8.7%.

2-Ethylmercapto-3-carbamoyl-4,6-diphenylpyridine (IX). A mixture of 1.58 g (5 mmole) of alkyl derivative VIf and 10 ml of concentrated H_2SO_4 was heated on a water bath for 5 h, after which it was cooled and poured into water. The precipitate was removed by filtration to give 1.42 g (85%) of VIII with mp 191-193°C (from ethanol). IR spectrum: 3380, 3270 (NH_2); 1647 cm^{-1} (C=O). Found: C 71.9; H 5.4; N 7.7; S 9.3%. $C_{20}H_{16}N_2OS$. Calculated: C 71.8; H 5.4; N 8.4; S 9.6%.

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PREPARATION OF α- AND γ-(α-FURYL)PYRIDINES

N. S. Prostakov, P. K. Radzhan, A. T. Soldatenkov, and A. I. Mikaya

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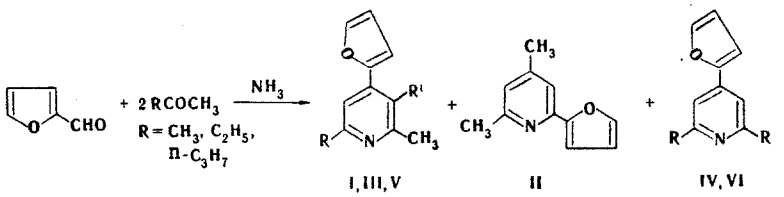
Mixtures of isomeric alkyl-substituted (in the pyridine ring) α- and γ-(α-furyl)-pyridines were obtained in up to ~40% yields by condensation of furfural and ammonia with several aliphatic ketones and aldehydes (at 370-380°C with a cadmium calcium phosphate catalyst). The dependence of the yields and structures of the corresponding isomers on the structure of the starting carbonyl compound was examined. Data from the PMR and mass spectra were used to prove the structures of the pyridine bases obtained.

In series of heteroaryl-substituted pyridine bases furylpyridines remain relatively little-studied and difficult-to-obtain compounds; this is due to the limitations involved in the methods for their synthesis [1, 2]. The interest in furylpyridines is due to the fact that substances that have high and diverse biological activity are found among them [2, 3]. Continuing our research on the chemistry of pyridine bases we turned to the synthesis of α- and γ-(α-furyl)pyridines by the Chichibabin method [4] by condensation of furfural and ammonia with ketones (acetone, methyl ethyl ketone, and methyl n-propyl ketone) and aldehydes (acetaldehyde, propionaldehyde, butyraldehyde, and crotonaldehyde). The condensation was carried out in the vapor phase at 370-380°C in the presence of a cadmium calcium phosphate catalyst.

Mixtures of primarily two isomers of furyl-substituted pyridines in overall yields up to 40% with various isomer ratios are formed in the condensation of furfural and ammonia with these carbonyl compounds. The structures of the isomers and their quantitative ratios depend on the structure of the starting carbonyl compound.



I, III, V II IV, VI

I $R = CH_3$; $R' = H$; III, IV $R = C_2H_5$; III $R' = CH_3$; V, VI $R = n\text{-}C_3H_7$; V $R' = C_2H_5$

Patrice Lumumba People's Friendship University, Moscow 117923.

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