

# Three-Component Synthesis of Alkyl-Substituted Functionalized 4*H*-Thiopyrans, 1,2- and 1,4-Dihydropyridines, 2-Alkylsulfanylpyridines, Thieno[2,3-*b*]pyridines, and Cyclohexa-1,3-diene

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Received January 19, 2015

**Abstract**—Three-component condensation of aliphatic aldehydes with CH-acids has afforded functionalized alkyl-substituted 4*H*-thiopyrans, 1,2- and 1,4-dihydropyridines, 2-alkylsulfanylpyridines, thieno[2,3-*b*]pyridines, and cyclohexa-1,3-diene.

**Keywords:** aliphatic aldehyde, CH-acid, 4*H*-thiopyran, 1,4-dihydropyridine, thieno[2,3-*b*]pyridine, cyclohexa-1,3-diene

**DOI:** 10.1134/S1070363215050102

Multicomponent synthesis of heterocyclic compounds has recently become increasingly important [1–3]. This method is particularly relevant to obtain scarcely studied alkyl-substituted carbo- and heterocyclic compounds starting from aliphatic aldehydes, since the latter are known for high toxicity, flammability, and ability to readily isomerize and dimerize [4] as compared with the aromatic analogs.

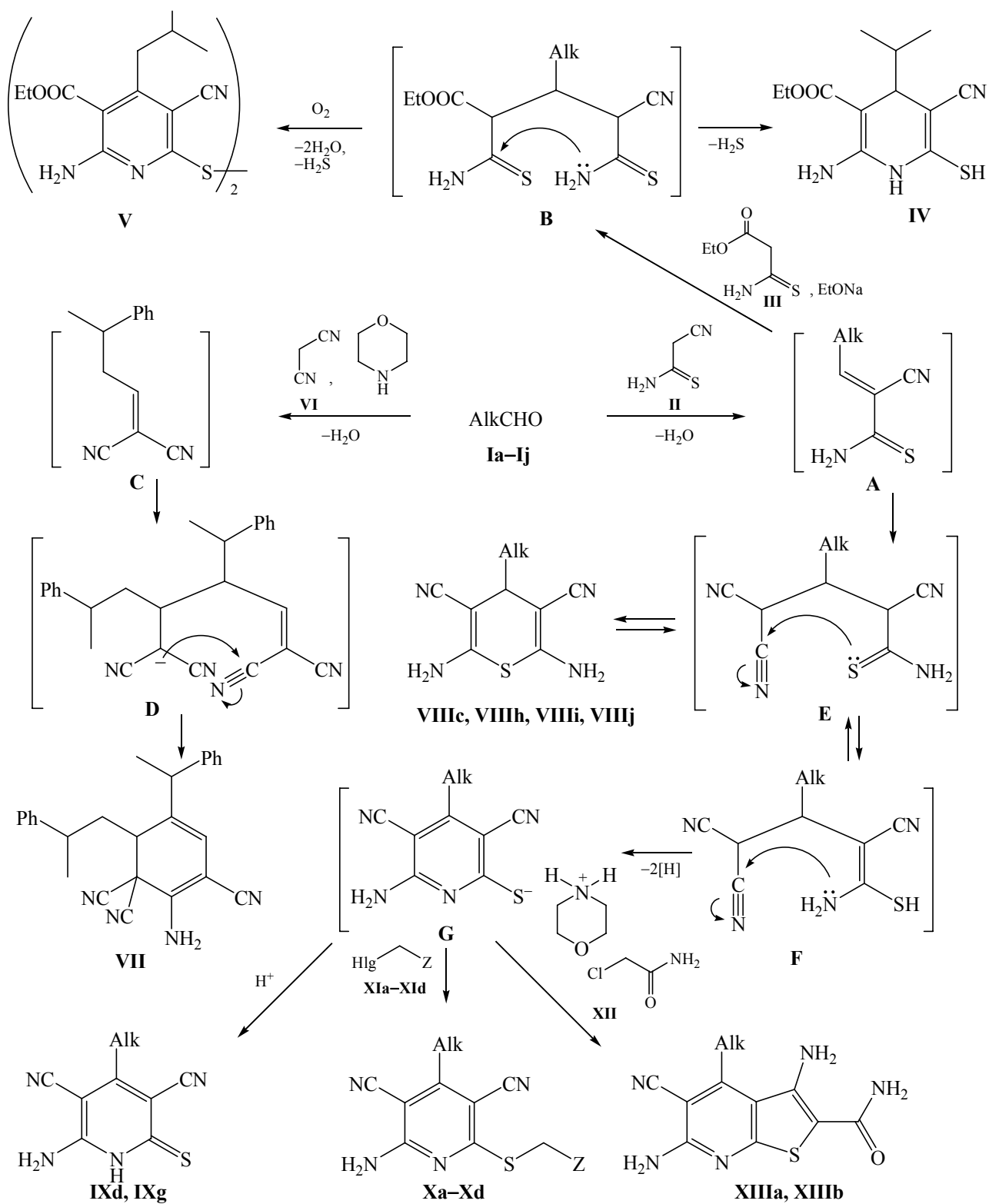
Extending the earlier research on synthesis of alkyl-substituted carbo- and heterocyclic compounds via a multicomponent condensation [5–7], we investigated new possibilities of three-component interaction of aliphatic aldehydes **Ia–Ij** with a number of CH-acids and organic bases under conditions of the Knöevenagel reaction. It was found that condensation of aliphatic aldehydes **Ia** and **Ib** with cyanothioacetamide **II** and ethyl 3-amino-3-thioxopropanoate **III** in anhydrous ethanol at 20°C in the presence of sodium ethylate resulted in ethyl 2-amino-4-isopropyl-6-mercapto-5-cyano-3-carboxylate **IV** and diethyl 6,6'-disulfandiylbis(2-amino-4-isobutyl-5-cyanonicotinate **V**. Apparently, the reaction proceeded through formation of alkene **A** followed by addition of the CH-acid **III** to give the adduct **B**. The latter intermediate [Alk = (Me)<sub>2</sub>CH] underwent chemoselective intramolecular cyclization accompanied with hydrogen sulfide elimination to

form the substituted 1,4-dihydropyridine **IV**. In the case of Alk = (Me)<sub>2</sub>CHCH<sub>2</sub>, the reaction stopped at the stage of formation of the corresponding 1,4-dihydropyridine **IV** due to oxidation of the hydrosulfide group with air oxygen into organic disulfide **V**. On top of that, the reaction was accompanied with aromatization of the dihydropyridine core (Scheme 1).

In the case of the Knöevenagel condensation involving 2-phenylpropionaldehyde **Ic** and malononitrile **VI** in the presence of morpholine as a catalyst, the formed alkene **C** was capable of the Michael-type dimerization under the reaction conditions. The adduct **D** underwent intramolecular cyclization into the substituted 1,3-cyclohexadiene **VII**.

Three-component condensation of aliphatic aldehydes **I** with cyanothioacetamide **II** and malononitrile **VI** in the presence of morpholine in anhydrous ethanol at 20°C resulted in the formation of 4-alkyl-2,6-diamino-3,5-dicyano-4*H*-thiopyrans **VIIIc**, **VIIIh**, **VIIIi**, and **VIIIj**. At the same time, the same reaction in ethanol medium under reflux allowed preparation of 4-substituted 6-amino-2-thioxo-3,5-dicyano-1,2-dihydropyridines **IXd** and **IXg**, similarly to the analogous condensation involving aromatic aldehydes [8–10]. Thiopyrans **VIII**, the kinetic control products, underwent ring-opening via formation of intermediates

Scheme 1.



**I, VIII, IX, XIII**, Alk = (Me)<sub>2</sub>CH (**a**), (Me)<sub>2</sub>CHCH<sub>2</sub> (**b**), Me(Ph)CH (**c**), Me(Ph)CHCH<sub>2</sub> (**d**), cyclohex-2-enyl (**e**), Me(CH<sub>2</sub>)<sub>10</sub> (**f**), Ph(CH<sub>2</sub>)<sub>2</sub> (**g**), Me(CH<sub>2</sub>)<sub>6</sub> (**h**), PhCH<sub>2</sub> (**i**), Me(CH<sub>2</sub>)<sub>5</sub> (**j**); **X, XI**, Hlg = Cl, Z = Ph, Alk = cyclohex-2-enyl (**a**); Hlg = Br, Z = 4-ClC<sub>6</sub>H<sub>4</sub>CO, Alk = Me(CH<sub>2</sub>)<sub>10</sub> (**b**); Hlg = Br, Z = 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CO, Alk = PhCH<sub>2</sub> (**c**); Hlg = I, Z = H, Alk = CH<sub>2</sub>Ph (**d**).

**Table 1.** Yields, melting points and elemental analysis data for compounds **IV–X** and **XIII**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
<b>IV</b>	65	197–199 (EtOH)	53.84	6.29	15.65	C <sub>12</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S	53.91	6.41	15.72
<b>V</b>	69	263–265 (AcOH)	55.98	5.63	14.92	C <sub>26</sub> H <sub>32</sub> N <sub>6</sub> O <sub>4</sub> S <sub>2</sub>	56.10	5.79	15.10
<b>VII</b>	72	218–220 (PrOH)	79.44	6.02	14.15	C <sub>26</sub> H <sub>24</sub> N <sub>4</sub>	79.48	6.22	14.30
<b>VIIIc</b>	80	206–208 (EtOH)	63.72	4.89	19.76	C <sub>15</sub> H <sub>14</sub> N <sub>4</sub> S	63.81	5.00	19.84
<b>VIIIh</b>	75	165–167 (EtOH)	60.70	7.15	20.12	C <sub>14</sub> H <sub>20</sub> N <sub>4</sub> S	60.84	7.29	20.27
<b>VIIIi</b>	77	183–185 (EtOH)	62.58	4.43	20.76	C <sub>14</sub> H <sub>12</sub> N <sub>4</sub> S	62.66	4.51	20.88
<b>VIIIj</b>	70	159–161 (PrOH)	57.84	6.60	20.71	C <sub>13</sub> H <sub>18</sub> N <sub>4</sub> S	57.97	6.74	20.80
<b>IXd</b>	66	233–235 (EtOH)	65.19	4.68	18.95	C <sub>16</sub> H <sub>14</sub> N <sub>4</sub> S	65.28	4.79	19.03
<b>IXg</b>	68	118–120 (MeOH)	64.18	4.21	19.86	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> S	64.26	4.32	19.98
<b>Xa<sup>a</sup></b>	71	162–163 (AcOH)	69.28	5.18	16.02	C <sub>20</sub> H <sub>18</sub> N <sub>4</sub> S	69.34	5.24	16.17
<b>Xb</b>	89	188–190 (AcOH)	64.58	6.32	11.49	C <sub>26</sub> H <sub>31</sub> ClN <sub>4</sub> OS	64.65	6.47	11.60
<b>Xc</b>	73	203–205 (BuOH)	61.48	3.46	16.22	C <sub>22</sub> H <sub>15</sub> N <sub>5</sub> O <sub>3</sub> S	61.53	3.52	16.31
<b>Xd</b>	82	241–243 (AcOH)	64.11	4.22	19.86	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> S	64.26	4.31	19.98
<b>XIIIa<sup>b</sup></b>	78	281–282 (AcOH)	52.26	4.68	25.30	C <sub>12</sub> H <sub>13</sub> N <sub>5</sub> OS	52.35	4.76	25.44
<b>XIIIb<sup>a</sup></b>	65	289–290 (BuOH)	53.86	5.15	24.03	C <sub>13</sub> H <sub>15</sub> N <sub>5</sub> OS	53.96	5.23	24.20

<sup>a</sup> Fluoresced under UV irradiation. <sup>b</sup> Sublimated at 200°C.

**E** and **F** to yield the substituted morpholinium pyridine-2-thiolates **G**. They were stabilized into pyridinethiones **IX** in acidic medium. Formation of the salts **G** was confirmed by formation of thioethers **X** when alkyl halides **XIa–XIId** were introduced in the reaction, in accordance with fundamentals of pyridinethiones chemistry [11–13]. Noteworthy, compounds **Xa–Xd** are promising building blocks to create drugs for treatment of inflammatory processes [14] and cardiovascular diseases [15].

When  $\alpha$ -chloroacetamide **XII** was used as alkylating agent in the presence of equimolar amount of 10% aqueous KOH, the reaction led to formation of 4-alkylthieno[2,3-*b*]pyridines **VIIIa** and **VIIIb**, showing potential antiviral [16, 17] and antitumor [18, 19] activity. Apparently, the reaction intermediates were the corresponding thioesters **X**, undergoing intramolecular cyclization in alkaline medium to form compounds **XIII**. 2-Alkylthio-3-cyanopyridine are convenient starting reagents for thieno[2,3-*b*]pyridines synthesis [20].

Spectral and physico-chemical properties of the synthesized compounds are shown in Tables 1 and 2.

In particular, IR spectra of the obtained compounds contained the expected characteristic absorption bands of NH<sub>2</sub> (3099–3450 cm<sup>-1</sup>), C≡N (1706–1724 cm<sup>-1</sup>), and C=O (2172–2252 cm<sup>-1</sup>) groups stretching. GC–MS spectra revealed the presence of the [M + 1]<sup>+</sup> molecular ion peak. Mass spectrum of compound **IXg** contained the molecular ion peak and peaks of other fragments including the [M + 2]<sup>+</sup> peak confirming the presence of one sulfur atom in the molecule [21]. The <sup>1</sup>H NMR spectra contained the signals of all the expected structural fragments.

## EXPERIMENTAL

IR spectra were recorded with a Perkin Elmer Spectrum One spectrophotometer (KBr pellets). <sup>1</sup>H NMR spectra were obtained using a Bruker Avance II (400.13 MHz) spectrometer (solutions in DMSO-*d*<sub>6</sub>) relative to TMS as internal reference. Mass spectra were registered with a Chrommass GC/MC (Hewlett Packard) 5890/5972 mass spectrometer [column HP-5 MS (70 eV)] (in the cases of CH<sub>2</sub>Cl<sub>2</sub> solutions) and with a Kratos MS-890 spectrometer (70 eV) with the direct specimen injection the ion source (**VII**, **IXb**,

**Table 2.** IR and <sup>1</sup>H NMR spectral data for compounds **IV–X** and **XIII**

Comp. no.	$\nu$ , cm <sup>-1</sup>	$\delta_{\text{H}}$ , ppm, ( <i>J</i> , Hz)
<b>IV</b>	3411, 3320, 3312, 3099 (NH, NH <sub>2</sub> ), 2172 (C≡N), 1724 (C=O), 1642 [ $\delta$ (NH <sub>2</sub> )]	0.89 d (6H, 2Me, <i>J</i> 6.6), 1.18 t (3H, CH <sub>2</sub> CH <sub>3</sub> , <i>J</i> 7.0), 1.51–1.66 m (1H, CHMe <sub>2</sub> ), 3.93 d (1H, C <sup>4</sup> H, <i>J</i> 4.3), 4.14 q (2H, OCH <sub>2</sub> , <i>J</i> 7.0), 6.17 br. s (2H, NH <sub>2</sub> ), 11.71 br. s (1H, NH); the signal of SH proton was not observed presumably due to the rapid deuterium exchange
<b>V</b>	3435, 3351, 3221 (NH <sub>2</sub> ), 2215 (C≡N), 1706 (C=O), 1632 [ $\delta$ (NH <sub>2</sub> )]	0.89 d (12H, 4Me, <i>J</i> 6.2), 1.35 t (6H, 2MeCH <sub>2</sub> , <i>J</i> 6.6), 1.76–1.92 m (2H, 2CHMe <sub>2</sub> ), 2.79 d (2H, 2CH <sub>2</sub> CH, <i>J</i> 6.8), 4.36 q (4H, 2OCH <sub>2</sub> , <i>J</i> 6.6), 7.20 br. s (4H, 2NH <sub>2</sub> )
<b>VII</b>	3450, 3340, 3215 (NH <sub>2</sub> ), 2252, 2200 (C≡N), 1644 [ $\delta$ (NH <sub>2</sub> )]	1.19 d (3H, Me, <i>J</i> 6.6), 1.33 d (3H, Me, <i>J</i> 6.5), 1.71–1.83 m (1H, CHMe), 2.18 q (1H, CHMe, <i>J</i> 6.5), 2.87 d (2H, CH <sub>2</sub> CH, <i>J</i> 6.7), 3.38 t (1H, C <sup>6</sup> H, <i>J</i> 6.8), 6.05 s (1H, C <sup>4</sup> H), 6.82–6.99 m (2H, Ph), 7.06–7.19 m (3H, Ph), 7.23–7.38 m (3H, Ph), 7.42 t (2H, Ph, <i>J</i> 8.1), 7.55 br. s (2H, NH <sub>2</sub> )
<b>VIIIc</b>	3444, 3314, 3210 (NH <sub>2</sub> ), 2202 (C≡N), 1647 [ $\delta$ (NH <sub>2</sub> )]	1.28 d (3H, Me, <i>J</i> 6.9), 2.81–3.04 m (1H, CHMe), 3.05 d (1H, C <sup>4</sup> H, <i>J</i> 5.8), 6.70 br. s (2H, NH <sub>2</sub> ), 6.85 br. s (2H, NH <sub>2</sub> ), 7.11–7.43 m (5H, Ph)
<b>VIIIh</b>	3440, 3295, 3202 (NH <sub>2</sub> ), 2204 (C≡N), 1643 [ $\delta$ (NH <sub>2</sub> )]	0.86 t (3H, Me, <i>J</i> 7.1), 1.08–1.55 m (10H, 5CH <sub>2</sub> ), 2.99 t (1H, C <sup>4</sup> H, <i>J</i> 6.9), 6.75 br. s (4H, 2NH <sub>2</sub> )
<b>VIIIi</b>	3435, 3302, 3215 (NH <sub>2</sub> ), 2200 (C≡N), 1642 [ $\delta$ (NH <sub>2</sub> )]	2.73 d (2H, CH <sub>2</sub> , <i>J</i> 6.4), 3.38 t (1H, C <sup>4</sup> H, <i>J</i> 6.4), 6.75 br. s (4H, 2NH <sub>2</sub> ), 7.02–7.46 m (5H, Ph)
<b>VIIIj</b>	3401, 3333, 3219 (NH <sub>2</sub> ), 2199 (C≡N), 1649 [ $\delta$ (NH <sub>2</sub> )]	1.92 t (3H, Me, <i>J</i> 6.8), 1.18–1.42 m (8H, 4CH <sub>2</sub> ), 1.48–1.64 m (2H, CH <sub>2</sub> ), 2.93 t (1H, C <sup>4</sup> H, <i>J</i> 7.2), 6.53 br. s (4H, 2NH <sub>2</sub> )
<b>IXd</b>	3418, 3311, 3209 (NH, NH <sub>2</sub> ), 2216 (C≡N), 1640 [ $\delta$ (NH <sub>2</sub> )]	1.31 d (3H, Me, <i>J</i> 7.2), 3.92–3.51 m (1H, CHMe), 3.61–4.01 m (2H, CH <sub>2</sub> ), 7.02–7.43 m (5H, Ph), 10.02 br. s (2H, NH <sub>2</sub> ), 11.82 br. s (1H, NH)
<b>IXg</b>	3402, 3300, 3196 (NH, NH <sub>2</sub> ), 2217 (C≡N), 1647 [ $\delta$ (NH <sub>2</sub> )]	2.71–3.11 m (4H, 2CH <sub>2</sub> ), 7.04–7.48 m (5H, Ph), 7.81 br. s (2H, NH <sub>2</sub> ), 12.71 br. s (1H, NH)
<b>Xa</b>	3446, 3334, 3216 (NH <sub>2</sub> ), 2214 (C≡N), 1624 [ $\delta$ (NH <sub>2</sub> )]	1.65–1.82 m (1H, C <sup>6</sup> H, cyclohexene), 2.04–2.33 m (5H, cyclohexene), 3.01–3.14 m (1H, C <sup>1</sup> H, cyclohexene), 4.45 s (2H, SCH <sub>2</sub> ), 5.66–5.79 m (2H, CH=CH), 7.23 d (1H, Ph, <i>J</i> 6.9), 7.29 t (2H, Ph, <i>J</i> 6.9), 7.47 d (2H, Ph, <i>J</i> 7.1), 7.94 br. s (2H, NH <sub>2</sub> )
<b>Xb</b>	3435, 3312, 3198 (NH <sub>2</sub> ), 2219 (C≡N), 1714 (C=O), 1648 [ $\delta$ (NH <sub>2</sub> )]	0.87 t (3H, Me, <i>J</i> 7.1), 1.06–1.52 m (16H, 8CH <sub>2</sub> ), 1.55–1.78 m (2H, CH <sub>2</sub> ), 2.72 t (2H, CH <sub>2</sub> , <i>J</i> 7.7), 4.83 s (2H, SCH <sub>2</sub> ), 7.53 d (2H, Ar, <i>J</i> 8.6), 7.64 br. s (2H, NH <sub>2</sub> ), 8.05 d (2H, Ar, <i>J</i> 8.6)
<b>Xc</b>	3430, 3318, 3206 (NH <sub>2</sub> ), 2220 (C≡N), 1706 (C=O), 1641 [ $\delta$ (NH <sub>2</sub> )]	4.11 s (2H, CH <sub>2</sub> ), 4.99 s (2H, SCH <sub>2</sub> ), 7.16–7.43 m (5H, Ph), 7.81 br. s (2H, NH <sub>2</sub> ), 8.22 d (2H, C <sub>6</sub> H <sub>4</sub> , <i>J</i> 8.4), 8.38 d (2H, C <sub>6</sub> H <sub>4</sub> , <i>J</i> 8.4)
<b>Xd</b>	3438, 3302, 3190 (NH <sub>2</sub> ), 2222 (C≡N), 1643 [ $\delta$ (NH <sub>2</sub> )]	2.54 s (3H, Me), 4.07 s (2H, CH <sub>2</sub> ), 7.14–7.46 m (5H, Ph), 7.96 br. s (2H, NH <sub>2</sub> )
<b>XIIIa</b>	3398, 3326, 3174 (NH <sub>2</sub> ), 2216 (C≡N), 1662 (CONH), 1634 [ $\delta$ (NH <sub>2</sub> )]	1.02 d (6H, 2Me, <i>J</i> 5.3), 2.08–2.19 m (1H, CHMe <sub>2</sub> ), 6.58 s (2H, NH <sub>2</sub> ), 6.66 s (2H, NH <sub>2</sub> ), 6.75 s (2H, NH <sub>2</sub> )
<b>XIIIb</b>	3390, 3338, 3206 (NH <sub>2</sub> ), 2219 (C≡N), 1670 (CONH), 1641 [ $\delta$ (NH <sub>2</sub> )]	1.12 d (6H, 2Me, <i>J</i> 5.8), 2.06–2.24 m (1H, CHMe <sub>2</sub> ), 2.93 d (2H, CH <sub>2</sub> , <i>J</i> 6.3), 6.58 s (2H, NH <sub>2</sub> ), 6.63 s (2H, NH <sub>2</sub> ), 6.76 s (2H, NH <sub>2</sub> )

**IXg**, and **Xb**). Melting points were determined with a Kofler device. The reaction progress was monitored with TLC on Silufol UV-254 plates, eluting with an acetone–hexane mixture (3 : 5) and developing with iodine vapor or UV irradiation.

**Ethyl 2-amino-4-isopropyl-6-thio-5-cyano-1,4-dihydropyridine-3-carboxylate (IV)**. 1.0 g (10 mmol) of cyanothioacetamide **II** and a solution of sodium ethylate prepared from 0.23 g (10 mmol) of sodium and 15 mL of anhydrous ethanol were added to a

solution of 0.91 mL (10 mmol) of isobutyral **Ia** in 15 mL of anhydrous ethanol at 20°C. The reaction mixture was stirred during 5 min, then 1.5 g (10 mmol) of CH-acid **III** was added, and the mixture was stirred during 30 min and incubated during 48 h. Next, the mixture was diluted with 10% hydrochloric acid to pH 5 upon stirring and incubated at room temperature during 48 h. The formed precipitate was filtered off and washed sequentially with water, ethanol, and hexane (Tables 1 and 2). Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 266 (100)  $[M - 1]^+$ .

**Diethyl 6,6'-disulfanediybis(2-amino-4-isobutyl-5-cyanonicotinate) (V)** was prepared similarly from 1.1 mL (10 mmol) of isovaleric aldehyde **Ib**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 557 (100)  $[M + 1]^+$ .

**2-Amino-6-(2-phenylpropyl)-5-(1-phenylethyl)-cyclohexa-2,4-diene-1,1,3-tricarbonitrile (VII)**. 3 drops of morpholine were added to a solution of 1.5 mL (10 mmol) of 3-phenylbutyral **Id** and 0.66 g (10 mmol) of malononitrile **VI** in 20 mL of anhydrous ethanol at 20°C. The reaction mixture was stirred during 1 h and incubated during 48 h. The formed precipitate was filtered off and washed with ethanol and hexane. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 394 (5)  $[M + 2]^+$ , 393 (18)  $[M + 1]^+$ , 392 (39)  $[M]^+$ , 287 (13)  $[M - PhCHMe]^+$ , 246 (12), 232 (11), 143 (18), 131 (10), 118 (32), 106 (49)  $[PhCH_2Me]^+$ , 105 (100)  $[PhCHMe]^+$ , 91 (54)  $[PhCH_2]^+$ , 79 (47)  $[C_6H_6+1]^+$ , 58 (42).

**4-Alkyl-2,6-diamino-3,5-dicyano-4H-thiopyrans (VIIIc, VIIIh, VIIIi, VIIIj) (general procedure)**. 3 drops of morpholine were added to a mixture of 10 mmol of the appropriate aldehyde **I** and 1.0 g (10 mmol) of cyanothioacetamide **II** in 20 mL of anhydrous ethanol at 20°C. The mixture was stirred during 1 h, and then 0.66 g (10 mmol) of malononitrile **VI** was added. The resulting mixture was stirred during 30 min and incubated during 24 h. The formed precipitate was filtered off and washed with ethanol and hexane (Tables 1 and 2).

**2,6-Diamino-4-(1-phenylethyl)-4H-thiopyran-3,5-dicarbonitrile (VIIIc)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 283 (100)  $[M + 1]^+$ .

**2,6-Diamino-4-heptyl-4H-thiopyran-3,5-dicarbonitrile (VIIIh)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 277 (100)  $[M + 1]^+$ .

**2,6-Diamino-4-benzyl-4H-thiopyran-3,5-dicarbonitrile (VIIIi)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 269 (100)  $[M + 1]^+$ .

**2,6-Diamino-4-hexyl-4H-thiopyran-3,5-dicarbonitrile (VIIIj)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 270 (100)  $[M + 1]^+$ .

**4-Alkyl-6-amino-2-thioxo-3,5-dicyano-1,2-dihydropyridines (IXd, IXg) (general procedure)**. 0.9 mL (10 mmol) of morpholine was added to a mixture of 10 mmol of the appropriate aldehyde **I** and 1.0 g (10 mmol) of cyanothioacetamide **II** in 20 mL of anhydrous ethanol at 20°C. The mixture was stirred during 30 min, and then 0.66 g (10 mmol) of malononitrile **VI** was added. The mixture was refluxed during 1 h, cooled, diluted with 10% hydrochloric acid to pH 5, and incubated during 48 h. The formed precipitate was filtered off and washed with ethanol and hexane (Tables 1 and 2).

**6-Amino-2-thioxo-4-(2-phenylpropyl)-1,2-dihydropyridine-3,5-dicarbonitrile (IXd)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 294 (8)  $[M]^+$ , 234 (11), 178 (9), 105 (100)  $[M - PhCHMe]^+$ , 91 (14)  $[PhCH_2]^+$ , 77 (22)  $[Ph]^+$ , 51 (12), 43 (24).

**6-Amino-2-thioxo-4-(2-phenylethyl)-1,2-dihydropyridine-3,5-dicarbonitrile (IXg)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 282 (4)  $[M + 2]^+$ , 281 (6)  $[M + 1]^+$ , 280 (29)  $[M]^+$ , 279 (9)  $[M - 1]^+$ , 203 (3), 162 (4), 91 (100)  $[PhCH_2]^+$ , 77 (4)  $[Ph]^+$ , 65 (11), 51 (3), 39 (3).

**4-Alkyl-6-amino-2-alkylsulfanyl-3,5-dicyanopyridines (Xa–Xd)** were prepared similarly from the appropriate alkyl halides **Xa–Xd** instead of hydrochloric acid.

**2-Amino-6-benzylsulfanyl-4-(cyclohex-3-en-1-yl)pyridine-3,5-dicarbonitrile (Xa)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 345 (100)  $[M - 1]^+$ .

**6-Amino-4-undecyl-2-(4-chlorobenzoylmethylsulfanyl)pyridine-3,5-dicarbonitrile (Xb)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 484 (3)  $[M + 1]^+$ , 483 (4)  $[M]^+$ , 482 (5)  $[M - 1]^+$ , 343 (6), 139 (100),  $[4-ClC_6H_4CO]^+$ , 125 (6), 111 (18), 43 (14).

**6-Amino-4-benzyl-2-(4-nitrobenzoylmethylsulfanyl)pyridine-3,5-dicarbonitrile (Xc)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 430 (100)  $[M + 1]^+$ .

**6-Amino-4-benzyl-2-methylsulfanylpyridine-3,5-dicarbonitrile (Xd)**. Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 281 (100)  $[M + 1]^+$ .

**Substituted thieno[2,3-*b*]pyridines (XIIIa, XIIIb)** were prepared similarly using 5.6 mL (10 mmol) of 10% aqueous solution of KOH and 0.94 g (10 mmol) of  $\alpha$ -chloroacetamide **XII** instead of hydrochloric acid.

**3,6-Diamino-4-isopropyl-5-cyanothieno[2,3-*b*]-pyridine-2-carboxamide (XIIIa).** Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 276 (100) [ $M + 1$ ]<sup>+</sup>.

**3,6-Diamino-4-isobutyl-5-cyanothieno[2,3-*b*]-pyridine-2-carboxamide (XIIIb).** Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 290 (100) [ $M + 1$ ]<sup>+</sup>.

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