

# Cross-Recyclization of 4-Aryl-2,6-diamino-4*H*-thiopyran-3,5-dicarbonitriles with 1-Morpholino-1-cyclopentene: New Route to 4-Aryl-2-thioxo-2,5,6,7-tetrahydro-1*H*-[1]pyrindine-3-carbonitriles and Their Derivatives

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**Abstract**—Reaction of 4-aryl-2,6-diamino-4*H*-thiopyran-3,5-dicarbonitriles with 1-morpholino-1-cyclopentene led to the formation of 4-aryl-2-thioxo-2,5,6,7-tetrahydro-1*H*-[1]pyrindine-3-carbonitriles used in the synthesis of substituted 2-alkylsulfanyl-4-aryl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitriles and 3-amino-4-aryl-6,7-dihydro-5*H*-cyclopenta[*b*]thieno[3,2-*e*]pyridines.

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The interest of researchers to pyrindine derivatives is aroused by discovery among them of compounds with antiphlogistic [1], antidepressant [2], anticonvulsant [3], and antibacterial activity [4]. The main synthetic procedures for the pyrindine skeleton consist in the condensation of sodium salts of cyclopentanone 2-formyl derivatives with cyanoacetic acid chalcogenoamides [5], recyclization of 4-amino-6-aryl-1,3-dithia-2-spirocyclopentane-5-cyano-4-cyclohexenes [6], reaction of 2,5-dibenzylidicyclopentanone with cyanothioacetamide [7], reaction of cyclohexylidencyanothioacetamide with 1-morpholino-1-cyclopentene [8], three-component condensation of aldehydes with cyanoacetic acid derivatives and cyclopentanone [9] or its enamine [10], and reaction of cyclopentanone dithioacetal with  $\beta$ -lithioaminoacrylonitrile [11].

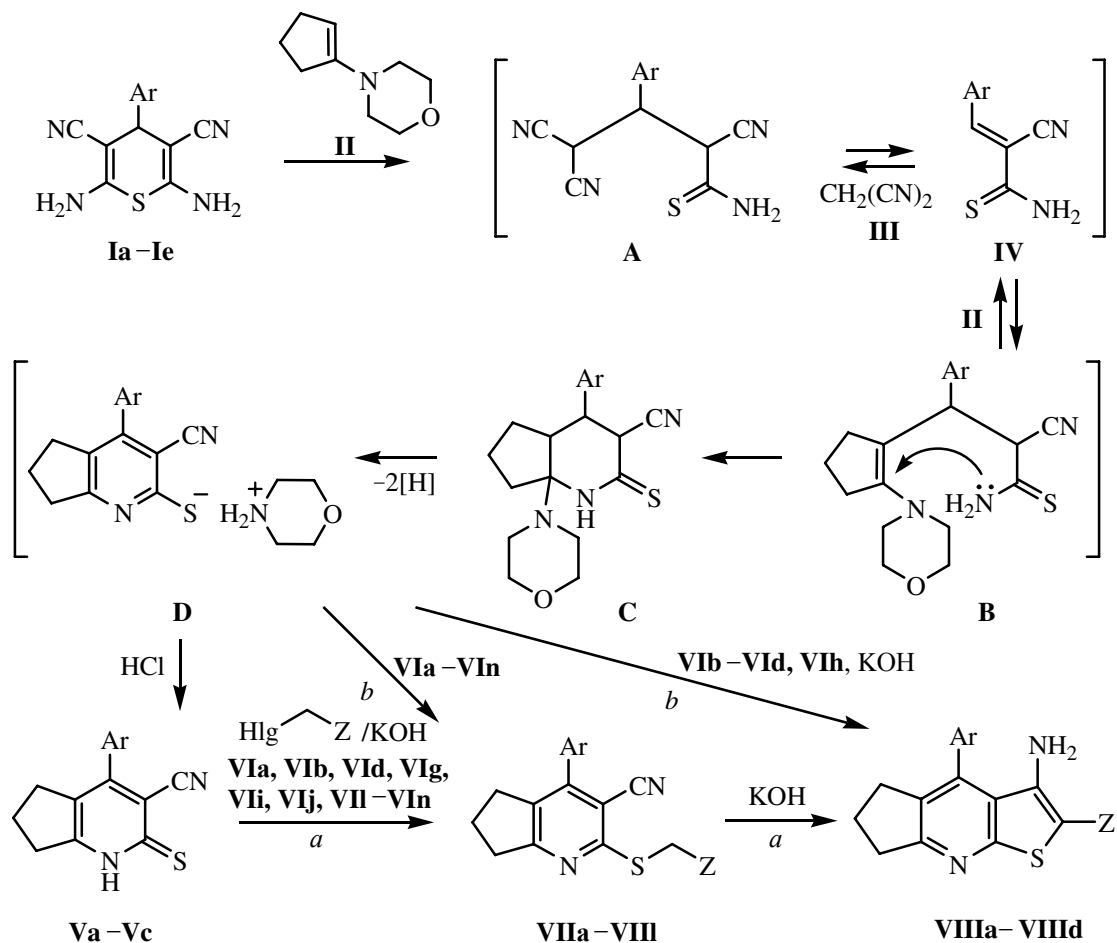
In this study a new route was discovered leading to compounds of these class involving a cross-recyclization of 4-aryl-2,6-diamino-4*H*-thiopyran-3,5-dicarbonitriles **Ia–Ie** with 1-morpholino-1-cyclopentene (**II**). The reaction pathway includes apparently the opening of the thiopyran ring giving intermediate **A** decomposing further into malononitrile (**III**) and arylmethylenecyanothioacetamide (**IV**). The latter reacts with enamine **II** by Stork reaction type [12] with the formation of adduct **B** undergoing intramolecular transamination and dehydration. As a result of these processes arise the corresponding structures **C**

and **D**. Further treating the mixture with hydrochloric acid provided 4-aryl-2-thioxo-2,5,6,7-tetrahydro-1*H*-[1]pyrindine-3-carbonitriles **Va–Vc**.

The structure of compounds **Va–Vc** was confirmed by spectral data and chemical reactions. For instance, their reaction with alkyl halides **VIa**, **VIb**, **VIc**, **VIg**, **VIh**, **VIj**, and **VII–VIIn** gives rise to the corresponding thioethers **VIIa–VIIi** (method *a*) which can be obtained in a one-pot synthesis omitting the stage of 2-thioxopyrindines **Va–Vc** isolation (method *b*).

2-Alkylsulfanyl-4-aryl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitriles **VIIb** and **VIIh** were transformed by treating with KOH into substituted 3-amino-4-aryl-6,7-dihydro-5*H*-cyclopenta[*b*]thieno[3,2-*e*]pyridines **VIIIa** and **VIIIb** (method *a*), a characteristic reaction of substituted heterocycles with the vicinal location of a nitrile and an alkylsulfanyl groups [13]. Compounds **VIIIa–VIIId** easily formed from the reaction mixture obtained by boiling in ethanol thiopyrans **Ia–Ie** and enamine **II**, at treating it in succession with alkyl halides **VIa–VIIn** and a water solution of KOH (method *b*).

IR spectra of thioethers **VIIa–VIII** contain characteristic absorption bands from the stretching vibrations of a conjugated cyano group at 2208–2222 cm<sup>-1</sup>. In going to compounds **VIIIa–VIIId** these band disappear, and appear absorption bands of stretching and bending



**I, V**, Ar=Ph (**a**), 4-ClC<sub>6</sub>H<sub>4</sub> (**b**), 4-BrC<sub>6</sub>H<sub>4</sub> (**c**), 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> (**d**), 4-Me<sub>2</sub>CHC<sub>6</sub>H<sub>4</sub> (**e**); **VI**, Hlg=Cl (**a-i**), Br (**l-m**), I (**n**); Z=CO<sub>2</sub>CHMe<sub>2</sub> (**a**), CONHPh (**b**), CN (**c**), CO<sub>2</sub>Me (**d**), CO<sub>2</sub>CH<sub>2</sub>Ph (**e**), CO<sub>2</sub>Ph (**f**), CONH<sub>2</sub> (**g**), 4-MeOC<sub>6</sub>H<sub>4</sub>NHCO (**h**), CO<sub>2</sub>Et (**i**), 4-ClC<sub>6</sub>H<sub>4</sub>CO (**j**), 2,4,5-Me<sub>3</sub>C<sub>6</sub>H<sub>2</sub>CO (**k**), COPh (**l**), CH=CH<sub>2</sub> (**m**), H (**n**); **VII**, Ar=Ph (**a**), 4-Me<sub>2</sub>CHC<sub>6</sub>H<sub>4</sub> (**b-e**), 4-ClC<sub>6</sub>H<sub>4</sub> (**f-i**), 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> (**j**), 4-BrC<sub>6</sub>H<sub>4</sub> (**k, l**); Z=CO<sub>2</sub>CHMe<sub>2</sub> (**a**), CONHPh (**b**), 4-ClC<sub>6</sub>H<sub>4</sub>CO (**c**), CO<sub>2</sub>Et (**d**), H (**e**), COPh (**f**), CH=CH<sub>2</sub> (**g**), CO<sub>2</sub>Me (**h**), CONH<sub>2</sub> (**i**), 2,4,5-Me<sub>3</sub>C<sub>6</sub>H<sub>2</sub>CO (**j**), CO<sub>2</sub>Ph (**k**), CO<sub>2</sub>CH<sub>2</sub>Ph (**l**); **VIII**, Ar=4-Me<sub>2</sub>CHC<sub>6</sub>H<sub>4</sub> (**a, d**), 4-ClC<sub>6</sub>H<sub>4</sub> (**b, c**); Z=CONHPh (**a**), CO<sub>2</sub>Me (**b**), 4-MeOC<sub>6</sub>H<sub>4</sub>NHCO (**c**), CN (**d**).

vibrations of amino group at 3195–3422 and 1640–1649 cm<sup>-1</sup> respectively. In the <sup>1</sup>H NMR spectra of compounds **VIIa-VIII** alongside the characteristic signals of aromatic protons, those of the trimethylene fragment, and Z (see EXPERIMENTAL), a signal of protons belonging to SCH<sub>2</sub> group appeared as a singlet in the region  $\delta$  3.95–4.88 ppm. At the same time the signals of SCH<sub>2</sub> group protons disappear from the spectra of compounds **VIIIa-VIII d**, and a signal of amino group protons is present instead at  $\delta$  5.33–5.83 ppm.

Note the resistance of compounds **VII** and **VIII** against electron impact as shown by the presence of molecular ion peaks in their mass spectra (see EXPERIMENTAL). Besides the numerical values of peaks correspond to the “nitrogen rule” [14] thus confirming the structure of compounds **VII** and **VIII**.

## EXPERIMENTAL

IR spectra were recorded on a spectrophotometer IKS-40 from mulls in mineral oil. <sup>1</sup>H NMR spectra were registered on spectrometers Bruker WP-100SY (100 MHz) (compounds **VIII k** and **VIII l**), Gemini-200 (199.975 MHz) (compound **VII a**), Varian Mercury-400 (400.397 MHz) (compounds **I e** and **VII j**), and Bruker DR-500 (500.13 MHz) (compounds **V c**, **VII b-VIII i**, and **VIII a-VIII d**) from solutions in DMSO-*d*<sub>6</sub> with TMS as an internal reference. Mass spectra were measured on KratosMS-890 instrument (70eV) with direct admission of samples into an ion source. Melting points were determined on a Koeffler heating block. The reactions progress was monitored and the purity of compounds obtained was checked by TLC on Silufol UV-254 plates,

eluent acetone–hexane, 3:5, development in iodine vapor or under UV irradiation.

Substituted 4*H*-thiopyrans **Ia–Ie** were obtained by method [15]. Compounds **Ia–Ic** were characterized in [15], **Id**, in [16].

**2,6-Diamino-4-(4-isopropylphenyl)-4*H*-thiopyran-3,5-dicarbonitrile (Ie)**. Yield 1.95 g (81%), white powder, mp 236–239°C (EtOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3465, 3327, 3190 ( $\text{NH}_2$ ), 2200 sh ( $\text{C}\equiv\text{N}$ ), 1650 [ $\delta(\text{NH}_2)$ ].  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.24 d (6H, 2Me,  $J$  7.12 Hz), 2.26 m (1H,  $\text{CHMe}_2$ ), 4.15 s (1H,  $\text{H}^d$ ), 6.54 br.s (4H, 2 $\text{NH}_2$ ), 7.16 d and 7.22 d (2H each,  $\text{C}_6\text{H}_4$ ,  $J$  7.13 Hz). Found, %: C 64.69; H 5.28; N 18.75.  $\text{C}_{16}\text{H}_{16}\text{N}_4\text{S}$ . Calculated, %: C 64.84; H 5.44; N 18.90.

**4-Aryl-2-thioxo-2,5,6,7-tetrahydro-1*H*-[1]pyridine-3-carbonitriles Va–Vc**. A mixture of 10 mmol of an appropriate 4*H*-thiopyran **Ia–Ic** and 1.53 g (10 mmol) of enamine **II** in 25 ml of anhydrous ethanol was boiled for 5 h. On cooling the reaction mixture was diluted with 10% hydrochloric acid till pH 5 and left standing for 48 h. Then the precipitate was filtered off and washed with ethanol and hexane.

**2-Thioxo-4-phenyl-2,5,6,7-tetrahydro-1*H*-[1]pyridine-3-carbonitrile (Va)**. Yield 1.64 g (65%), yellow powder, mp 240–242°C (AcOH) (239–240°C [17]).

**2-Thioxo-4-(4-chlorophenyl)-2,5,6,7-tetrahydro-1*H*-[1]pyridine-3-carbonitrile (Vb)**. Yield 1.72 g (60%), yellow powder, mp 262–264°C (AcOH) (259–261°C [17]).

**4-(4-Isopropylphenyl)-2-thioxo-2,5,6,7-tetrahydro-1*H*-[1]pyridine-3-carbonitrile (Vc)**. Yield 1.59 g (54%), yellow powder, mp 228–230°C (AcOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2216 ( $\text{C}\equiv\text{N}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.29 d (6H, 2Me,  $J$  6.94 Hz), 2.03 m (2H,  $\text{C}^6\text{H}_2$ ), 2.63 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.40 Hz), 3.03 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  4.60 Hz), 7.36 s (4H,  $\text{C}_6\text{H}_4$ ), 14.21 br.s (1H, NH). Found, %: C 73.29; H 6.01; N 9.38.  $\text{C}_{18}\text{H}_{18}\text{N}_2\text{S}$ . Calculated, %: C 73.43; H 6.16; N 9.52.

**4-Aryl-2-*Z*-methylsulfanyl-6,7-dihydro-5*H*-[1]pyridine-3-carbonitriles VIIa–VIIi**. *a*. To a stirred solution of 10 mmol of an appropriate 2-thioxopyridine **Va–Vc** in 15 ml of DMF was added at 20°C in succession 5.6 ml (10 mmol) of 10% water solution of KOH and 10 mmol of an appropriate alkyl halide **VIa**, **VIb**, **VIc**, **VIg**, **VIi**, **VIj**, or **VII–VIIn**, the mixture was stirred for 30 min and then diluted with an equal volume of water. The separated precipitate was filtered off, washed with water, ethanol, and hexane.

**2-Isopropylloxycarbonylmethylsulfanyl-4-phenyl-6,7-dihydro-5*H*-[1]pyridine-3-carbonitrile (VIIa)**. Yield 2.78 g (79%), yellow wool, mp 147°C (*i*-PrOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2218 ( $\text{C}\equiv\text{N}$ ), 1735 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.26 d (6H, 2Me,  $J$  6.30 Hz), 2.09 m (2H,  $\text{C}^6\text{H}_2$ ), 2.83 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.24 Hz), 3.02 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.89 Hz), 3.99 s (2H,  $\text{SCH}_2$ ), 4.95 m (1H,  $\text{CHMe}_2$ ), 7.41–7.62 m (5H, Ph). Found, %: C 67.95; H 5.61; N 7.82.  $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ . Calculated, %: C 68.16; H 5.72; N 7.95.

**4-(4-Isopropylphenyl)-2-phenylcarbonylmethylsulfanyl-6,7-dihydro-5*H*-[1]pyridine-3-carbonitrile (VIIb)**. Yield 2.99 g (70%), yellow powder, mp 164–165°C (AcOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2217 ( $\text{C}\equiv\text{N}$ ), 1672 ( $\text{CONH}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.26 d (6H, 2Me,  $J$  6.95 Hz), 2.07 m (2H,  $\text{C}^6\text{H}_2$ ), 2.82 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.18 Hz), 2.99 m (3H,  $\text{C}^7\text{H}_2$  and  $\text{CHMe}_2$ ), 4.19 s (2H,  $\text{SCH}_2$ ), 7.04 t (1H, Ph,  $J$  6.97 Hz), 7.29 t (2H, Ph,  $J$  6.97 Hz), 7.41 s (4H,  $\text{C}_6\text{H}_4$ ), 7.58 d (2H, Ph,  $J$  7.02 Hz), 10.16 br.s (1H, NH). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 427 (3) [ $M$ ]<sup>+</sup>, 335 (100) [ $M$ -PhNH]<sup>+</sup>, 307 (34), 291 (15), 279 (10), 265 (61), 190 (11), 106 (15), 93 (38) [ $\text{PhNH}_2$ ]<sup>+</sup>, 77 (26) [ $\text{Ph}$ ]<sup>+</sup>, 65 (22), 43 (15). Found, %: C 72.89; H 5.70; N 9.67.  $\text{C}_{26}\text{H}_{25}\text{N}_3\text{OS}$ . Calculated, %: C 73.04; H 5.89; N 9.83.  $M$  427.

**4-(4-Isopropylphenyl)-2-(4-chlorobenzoylmethylsulfanyl)-6,7-dihydro-5*H*-[1]pyridine-3-carbonitrile (VIIc)**. Yield 2.46 g (55%), yellow powder, mp 123–124°C (AcOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2215 ( $\text{C}\equiv\text{N}$ ), 1692 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.29 d (6H, 2Me,  $J$  6.92 Hz), 1.98 m (2H,  $\text{C}^6\text{H}_2$ ), 2.77 m (4H,  $\text{C}^5\text{H}_2$  and  $\text{C}^7\text{H}_2$ ), 2.97 m (1H,  $\text{CHMe}_2$ ), 4.81 s (2H,  $\text{SCH}_2$ ), 7.40 s (4H,  $\text{C}_6\text{H}_4$ ), 7.61 d and 8.15 d ( $\ddot{\text{O}}$  2H, 4- $\text{Cl}_6\text{H}_4$ ,  $J$  8.57 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 448 (4) [ $M + 1$ ]<sup>+</sup>, 447 (5) [ $M$ ]<sup>+</sup>, 446 (8) [ $M - 1$ ]<sup>+</sup>, 445 (6) [ $M - 2$ ]<sup>+</sup>, 307 (84), 265 (26), 139 (100), 111 (32), 75 (9), 43 (5). Found, %: C 69.72; H 5.04; N 6.12.  $\text{C}_{26}\text{H}_{23}\text{ClN}_2\text{OS}$ . Calculated, %: C 69.86; H 5.19; N 6.27.  $M$  447.

**4-(4-Isopropylphenyl)-2-ethoxycarbonylmethylsulfanyl-6,7-dihydro-5*H*-[1]pyridine-3-carbonitrile (VIIId)**. Yield 2.09 g (57%), white powder, mp 97–98°C (EtOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2219 ( $\text{C}\equiv\text{N}$ ), 1732 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.28 t (3H,  $\text{CH}_3\text{CH}_2$ ,  $J$  6.16 Hz), 1.31 d (6H, 2Me,  $J$  6.91 Hz), 2.07 m (2H,  $\text{C}^6\text{H}_2$ ), 2.83 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.14 Hz), 3.02 m (3H,  $\text{C}^7\text{H}_2$  and  $\text{CHMe}_2$ ), 4.09 s (2H,  $\text{SCH}_2$ ), 4.15 q (2H,  $\text{OCH}_2$ ,  $J$  6.16 Hz), 7.42 s (4H,  $\text{C}_6\text{H}_4$ ). Found, %: C 69.28; H 6.11; N 7.18.  $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2\text{S}$ . Calculated, %: C 69.44; H 6.36; N 7.36.

**4-(4-Isopropylphenyl)-2-methylsulfanyl-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIe).** Yield 2.03 g (66%), yellow powder, mp 95°C (EtOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2219 ( $\text{C}\equiv\text{N}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.28 d (6H, 2Me,  $J$  6.84 Hz), 2.07 m (2H,  $\text{C}^6\text{H}_2$ ), 2.61 s (3H, SMe), 2.82 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.17 Hz), 2.99 m (1H,  $\text{CHMe}_2$ ), 3.05 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.22 Hz), 7.40 s (4H,  $\text{C}_6\text{H}_4$ ). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 310 (4) [ $M + 2$ ]<sup>+</sup>, 309 (13) [ $M + 1$ ]<sup>+</sup>, 308 (46) [ $M$ ]<sup>+</sup>, 307 (100) [ $M - 1$ ]<sup>+</sup>, 277 (9), 265 (94), 190 (16), 138 (39), 115 (11), 91 (10), 77 (12), 63 (7), 41 (14). Found, %: C 73.78; H 6.42; N 8.89.  $\text{C}_{19}\text{H}_{20}\text{N}_2\text{S}$ . Calculated, %: C 73.99; H 6.54; N 9.08.  $M$  308.

**2-Benzoylmethylsulfanyl-4-(4-chlorophenyl)-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIf).** Yield 3.35 g (83%), yellow powder, mp 180°C (AcOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2222 ( $\text{C}\equiv\text{N}$ ), 1697 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.00 m (2H,  $\text{C}^6\text{H}_2$ ), 2.75 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.21 Hz), 2.84 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.15 Hz), 4.88 s (2H,  $\text{SCH}_2$ ), 7.48–7.62 m (6H<sub>arom</sub>), 7.67 t (1H<sub>arom</sub>,  $J$  6.91 Hz), 8.06 d (2H<sub>arom</sub>,  $J$  8.54 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 404 (5) [ $M$ ]<sup>+</sup>, 299 (27), 190 (8), 105 (100) [ $\text{PhCO}$ ]<sup>+</sup>, 77 (31) [ $\text{Ph}$ ]<sup>+</sup>, 51 (6). Found, %: C 68.04; H 4.07; N 6.78.  $\text{C}_{23}\text{H}_{17}\text{ClN}_2\text{OS}$ . Calculated, %: C 68.23; H 4.23; N 6.92.  $M$  404.

**2-Allylsulfanyl-4-(4-chlorophenyl)-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIg).** Yield 2.02 g (62%), yellow powder, mp 99–100°C (MeOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2219 ( $\text{C}\equiv\text{N}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.07 m (2H,  $\text{C}^6\text{H}_2$ ), 2.80 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.25 Hz), 3.06 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.61 Hz), 3.95 d (2H,  $\text{SCH}_2$ ,  $J$  6.55 Hz), 5.14 d (1H,  $=\text{CH}_2$ ,  $J_{\text{cis}}$  9.56 Hz), 5.35 d (1H,  $=\text{CH}_2$ ,  $J_{\text{trans}}$  17.38 Hz), 5.96 m (1H,  $\text{CH}=\text{}$ ), 7.50 d and 7.58 d (2H each,  $\text{C}_6\text{H}_4$ ). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 329 (8) [ $M + 2$ ]<sup>+</sup>, 328 (31) [ $M + 1$ ]<sup>+</sup>, 327 (46) [ $M$ ]<sup>+</sup>, 326 (84) [ $M - 1$ ]<sup>+</sup>, 325 (87) [ $M - 2$ ]<sup>+</sup>, 311 (100), 293 (42), 258 (27), 218 (22), 190 (38), 177 (15), 164 (26), 138 (14), 114 (8), 71 (6), 39 (28). Found, %: C 66.01; H 4.48; N 8.42.  $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{S}$ . Calculated, %: C 66.15; H 4.63; N 8.57.  $M$  327.

**2-Methoxycarbonylmethylsulfanyl-4-(4-chlorophenyl)-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIh).** Yield 2.43 g (68%), white powder, mp 135–137°C (MeOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2218 ( $\text{C}\equiv\text{N}$ ), 1730 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.08 m (2H,  $\text{C}^6\text{H}_2$ ), 3.80 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.21 Hz), 3.02 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.57 Hz), 3.68 s (3H, Me), 4.12 s (2H,  $\text{SCH}_2$ ), 7.52 d and 7.59 d (iO 2H,  $\text{C}_6\text{H}_4$ ,  $J$  8.47 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 360 (14) [ $M + 2$ ]<sup>+</sup>, 359 (28) [ $M +$

1]<sup>+</sup>, 358 (35) [ $M$ ]<sup>+</sup>, 357 (66) [ $M - 1$ ]<sup>+</sup>, 323 (10), 299 (100), 263 (40), 218 (19), 190 (37), 164 (20), 59 (21), 45 (14). Found, %: C 60.11; H 4.08; N 7.66.  $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_2\text{S}$ . Calculated, %: C 60.25; H 4.21; N 7.81.  $M$  359.

**2-Carbamoylmethylsulfanyl-4-(4-chlorophenyl)-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIi).** Yield 2.61 g (76%), white powder, mp 182–183°C (EtOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2208 ( $\text{C}\equiv\text{N}$ ), 1692 ( $\text{CONH}_2$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.09 m (2H,  $\text{C}^6\text{H}_2$ ), 2.78 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.15 Hz), 3.04 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.58 Hz), 3.95 s (2H,  $\text{SCH}_2$ ), 7.04 br.s and 7.96 br.s (1H each,  $\text{NH}_2$ ), 7.52 d and 7.59 d (2H each,  $\text{C}_6\text{H}_4$ ,  $J$  8.54 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 345 (8) [ $M + 2$ ]<sup>+</sup>, 344 (11) [ $M + 1$ ]<sup>+</sup>, 343 (19) [ $M$ ]<sup>+</sup>, 342 (21) [ $M - 1$ ]<sup>+</sup>, 326 (10), 299 (100), 263 (25), 218 (14), 190 (27), 164 (19), 44 (23). Found, %: C 59.18; H 3.96; N 12.04.  $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{OS}$ . Calculated, %: C 59.39; H 4.10; N 12.22.  $M$  344.

**Compounds VIIa–VIII. b.** A mixture of 10 mmol of an appropriate 4H-thiopyran **Ia–Ie** and 1.53 g (10 mmol) of enamine **II** in 25 ml of anhydrous ethanol was boiled for 5 h and filtered while hot through a folded paper filter. On cooling to room temperature to the reaction mixture was added at stirring 10 mmol of an appropriate alkyl halide **VIa–VIh**, the mixture was stirred for 4 h, diluted with an equal volume of water, and the formed precipitate was filtered off, washed with water, ethanol, and hexane. Compounds **VIIa–VIIi** are identical in melting point and chromatographic data to those obtained by method *a*. Yield 71 (a), 65 (b), 77 (c), 59 (d), 66 (e), 53 (f), 75 (g), 64 (h), 61% (i).

**2-(2,4,5-Trimethylbenzoylmethylsulfanyl)-4-(4-nitrophenyl)-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIj).** Yield 3.43 g (75%), yellow powder, mp 155–156°C (BuOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2220 ( $\text{C}\equiv\text{N}$ ), 1688 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.09 m (2H,  $\text{C}^6\text{H}_2$ ), 2.26 s (3H, Me), 2.30 s (3H, Me), 2.34 s (3H, Me), 2.59 t (2H,  $\text{C}^5\text{H}_2$ ,  $J$  7.19 Hz), 2.91 t (2H,  $\text{C}^7\text{H}_2$ ,  $J$  7.61 Hz), 4.62 s (2H,  $\text{SCH}_2$ ), 7.00 s (1H<sub>arom</sub>), 7.68 s (1H<sub>arom</sub>), 7.75 d and 8.38 d (2H each,  $\text{C}_6\text{H}_4$ ,  $J$  6.99 Hz). Found, %: C 68.11; H 4.92; N 8.98.  $\text{C}_{26}\text{H}_{23}\text{N}_3\text{O}_3\text{S}$ . Calculated, %: C 68.25; H 5.07; N 9.18.

**4-(4-Bromophenyl)-2-phenoxy carbonylmethylsulfanyl-6,7-dihydro-5H-[1]pyrindine-3-carbonitrile (VIIk).** Yield 2.56 g (55%), white powder, mp 190–192°C (AcOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2212 ( $\text{C}\equiv\text{N}$ ), 1733 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.82 m (2H,  $\text{C}^6\text{H}_2$ ), 2.85–3.16 m (4H,  $\text{C}^5\text{H}_2$  and  $\text{C}^7\text{H}_2$ ), 4.49 s (2H,  $\text{SCH}_2$ ), 7.02–7.41 m (4H<sub>arom</sub>), 7.52–7.64 m (3H<sub>arom</sub>),

7.80 d ( $2H_{\text{arom}}$ ,  $J$  8.76 Hz). Found, %: C 59.22; H 3.46; N 5.88.  $C_{23}H_{17}BrN_2O_2S$ . Calculated, %: C 59.36; H 3.68; N 6.02.

**2-Benzoyloxycarbonylmethylsulfanyl-4-(4-bromophenyl)-6,7-dihydro-5H-[1]pyridine-3-carbonitrile (VIII)**. Yield 3.26 g (68%), yellow wool, mp 185–187°C (ACOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2220 ( $C\equiv N$ ), 1729 ( $C=O$ ).  $^1H$  NMR spectrum,  $\delta$ , ppm: 2.73–3.11 m (6H,  $3CH_2$ ), 4.32 s (2H,  $SCH_2$ ), 5.16 s (2H,  $OCH_2$ ), 7.24–7.55 m ( $7H_{\text{arom}}$ ), 7.79 d ( $2H_{\text{arom}}$ ,  $J$  7.51 Hz). Found, %: C 59.89; H 3.78; N 5.65.  $C_{24}H_{19}BrN_2O_2S$ . Calculated, %: C 60.13; H 3.99; N 5.84.

**3-Amino-4-aryl-6,7-dihydro-5H-cyclopenta[b]thieno[3,2-*e*]pyridines VIIIa and VIIIb a**. To a stirred solution of 10 mmol of an appropriate thioether **VIIb** or **VIIIh** in 15 ml of DMF was gradually added at 18°C 5.6 ml (10 mmol) of 10% water solution of KOH, the mixture was stirred for 1 h and then diluted with an equal volume of water. The formed precipitate was filtered off, washed with water, ethanol, and hexane.

**3-Amino-4-(4-isopropylphenyl)-*N*-phenyl-6,7-dihydro-5H-cyclopenta[b]thieno[3,2-*e*]pyridine-2-carboxamide (VIIIa)**. Yield 2.52 g (59%), yellow powder, mp 244–245°C (EtOH–DMF, 1:1). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3412, 3333, 3214 ( $NH_2$ ), 1682 ( $CONH$ ), 1645 [ $\delta(NH_2)$ ].  $^1H$  NMR spectrum,  $\delta$ , ppm: 1.30 d (6H, 2Me,  $J$  6.96 Hz), 2.11 m (2H,  $C^6H_2$ ), 2.71 t (2H,  $C^5H_2$ ,  $J$  7.22 Hz), 3.00 m (1H,  $CHMe_2$ ), 3.09 t (2H,  $C^7H_2$ ,  $J$  7.60 Hz), 5.83 br.s (2H,  $NH_2$ ), 7.04 t (1H, Ph,  $J$  6.94 Hz), 7.28 t (2H, Ph,  $J$  6.94 Hz), 7.32 d (2H, Ph,  $J$  7.01 Hz), 7.43 d and 7.63 d (2H each,  $C_6H_4$ ,  $J$  6.62 Hz), 9.26 br.s (1H, NH). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 429 (5) [ $M + 2$ ]<sup>+</sup>, 428 (16) [ $M + 1$ ]<sup>+</sup>, 427 (47) [ $M$ ]<sup>+</sup>, 335 (100) [ $M - PhNH_2$ ]<sup>+</sup>, 264 (38), 119 (10), 93 (18) [ $PhNH_2$ ]<sup>+</sup>, 77 (6) [ $Ph$ ]<sup>+</sup>, 65 (14), 43 (12). Found, %: C 72.95; H 5.70; N 9.68.  $C_{26}H_{25}N_3OS$ . Calculated, %: C 73.04; H 5.89; N 9.83.  $M$  427.

**Methyl-3-amino-4-(4-chlorophenyl)-6,7-dihydro-5H-cyclopenta[b]thieno[3,2-*e*]pyridine-2-carboxamide (VIIIb)**. Yield 2.54 g (71%), yellow powder, mp 235–236°C (BuOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3422, 3312, 3195 ( $NH_2$ ), 1731 ( $C=O$ ), 1648 [ $\delta(NH_2)$ ].  $^1H$  NMR spectrum,  $\delta$ , ppm: 2.10 m (2H,  $C^6H_2$ ), 2.17 t (2H,  $C^5H_2$ ,  $J$  7.18 Hz), 3.06 t (2H,  $C^7H_2$ ,  $J$  7.65 Hz), 3.76 c (3H, Me), 5.72 br.s (2H,  $NH_2$ ), 7.44 d and 7.61 d (2H each,  $C_6H_4$ ,  $J$  8.53 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 360 (41) [ $M + 2$ ]<sup>+</sup>, 359 (23) [ $M + 1$ ]<sup>+</sup>, 358 (100) [ $M$ ]<sup>+</sup>, 325 (97), 297 (32), 263 (29), 190 (18), 177 (11), 163 (17), 145 (44), 131 (42), 117 (20), 59 (8). Found, %: C 60.12;

H 4.08; N 7.66.  $C_{18}H_{15}ClN_2O_2S$ . Calculated, %: C 60.25; H 4.21; N 7.81.  $M$  359.

**Compounds VIIIa–VIIId. b**. A mixture of 10 mmol of an appropriate 4*H*-thiopyran **Ic** or **Ie** and 1.53 g (10 mmol) of enamine **II** in 25 ml of anhydrous ethanol was boiled for 5 h and filtered while hot through a folded paper filter. On cooling to room temperature to the reaction mixture was added at stirring 10 mmol of an appropriate alkyl halide **VIIb–VIIc**, **VIIh**, the mixture was stirred for 4 h, diluted with 10 ml of DMF, and 5.6 ml (10 mmol) of 10% water solution of KOH was added, the stirring was continued for 2 h, and the mixture was left standing for 24 h, then diluted with an equal volume of water. The separated precipitate was filtered off, washed with water, ethanol, and hexane.

Compounds **VIIIa** and **VIIIb** are identical in melting point and chromatographic data to those obtained by method *a*. Yield 72 and 66% respectively.

**3-Amino-*N*-(4-methoxyphenyl)-4-(4-chlorophenyl)-6,7-dihydro-5H-cyclopenta[b]thieno[3,2-*e*]pyridine-2-carboxamide (VIIIc)**. Yield 3.05 g (68%), yellow powder, mp 235–237°C (ACOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3405, 3330, 3211 ( $NH_2$ ), 1684 ( $CONH$ ), 1640 [ $\delta(NH_2)$ ].  $^1H$  NMR spectrum,  $\delta$ , ppm: 2.11 m (2H,  $C^6H_2$ ), 3.34 t (2H,  $C^5H_2$ ,  $J$  7.17 Hz), 3.09 t (2H,  $C^7H_2$ ,  $J$  7.64 Hz), 3.75 s (3H, Me), 5.78 br.s (2H,  $NH_2$ ), 6.85 d and 7.52 d (2H, 4-MeOC<sub>6</sub>H<sub>4</sub>,  $J$  8.82 Hz), 7.42 d and 7.61 d (2H, 4-ClC<sub>6</sub>H<sub>4</sub>,  $J$  8.53 Hz), 9.19 br.s (1H, NH). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 450 (5) [ $M + 1$ ]<sup>+</sup>, 449 (18) [ $M$ ]<sup>+</sup>, 327 (68), 297 (7), 264 (39), 123 (100) [4-MeOC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>]<sup>+</sup>, 108 (10), 95 (8), 77 (4) [ $Ph$ ]<sup>+</sup>. Found, %: C 63.88; H 4.31; N 9.12.  $C_{24}H_{20}ClN_3O_2S$ . Calculated, %: C 64.07; H 4.48; N 9.34.  $M$  450.

**3-Amino-4-(4-isopropylphenyl)-6,7-dihydro-5H-cyclopenta[b]thieno[3,2-*e*]pyridine-2-carbonitrile (VIIId)**. Yield 1.70 g (57%), yellow powder, mp 201–203°C (ACOH). IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3403, 3311, 3199 ( $NH_2$ ), 2214 ( $C\equiv N$ ), 1649 [ $\delta(NH_2)$ ].  $^1H$  NMR spectrum,  $\delta$ , ppm: 1.30 d (6H, 2Me,  $J$  6.95 Hz), 2.10 m (2H,  $C^6H_2$ ), 2.69 t (2H,  $C^5H_2$ ,  $J$  7.19 Hz), 3.02 m (1H,  $CHMe_2$ ), 3.08 t (2H,  $C^7H_2$ ,  $J$  7.61 Hz), 5.33 br.s (2H,  $NH_2$ ), 7.34 d and 7.45 d (2H each  $C_6H_4$ ,  $J$  6.81 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 335 (8) [ $M + 2$ ]<sup>+</sup>, 334 (25) [ $M + 1$ ]<sup>+</sup>, 333 (100) [ $M$ ]<sup>+</sup>, 332 (4) [ $M - 1$ ]<sup>+</sup>, 318 (15), 290 (21), 159 (22), 77 (6) [ $Ph$ ]<sup>+</sup>, 41 (4). Found, %: C 71.95; H 5.60; N 12.46.  $C_{20}H_{19}N_3S$ . Calculated, %: C 72.04; H 5.74; N 12.60.  $M$  333.

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