ISSN 1070-4280, Russian Journal of Organic Chemistry, 2007, Vol. 43, No. 2, pp. 280–285. © Pleiades Publishing, Ltd. 2007.
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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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Received October 4, 2005

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.

DOI: 10.1134/S1070428007020212

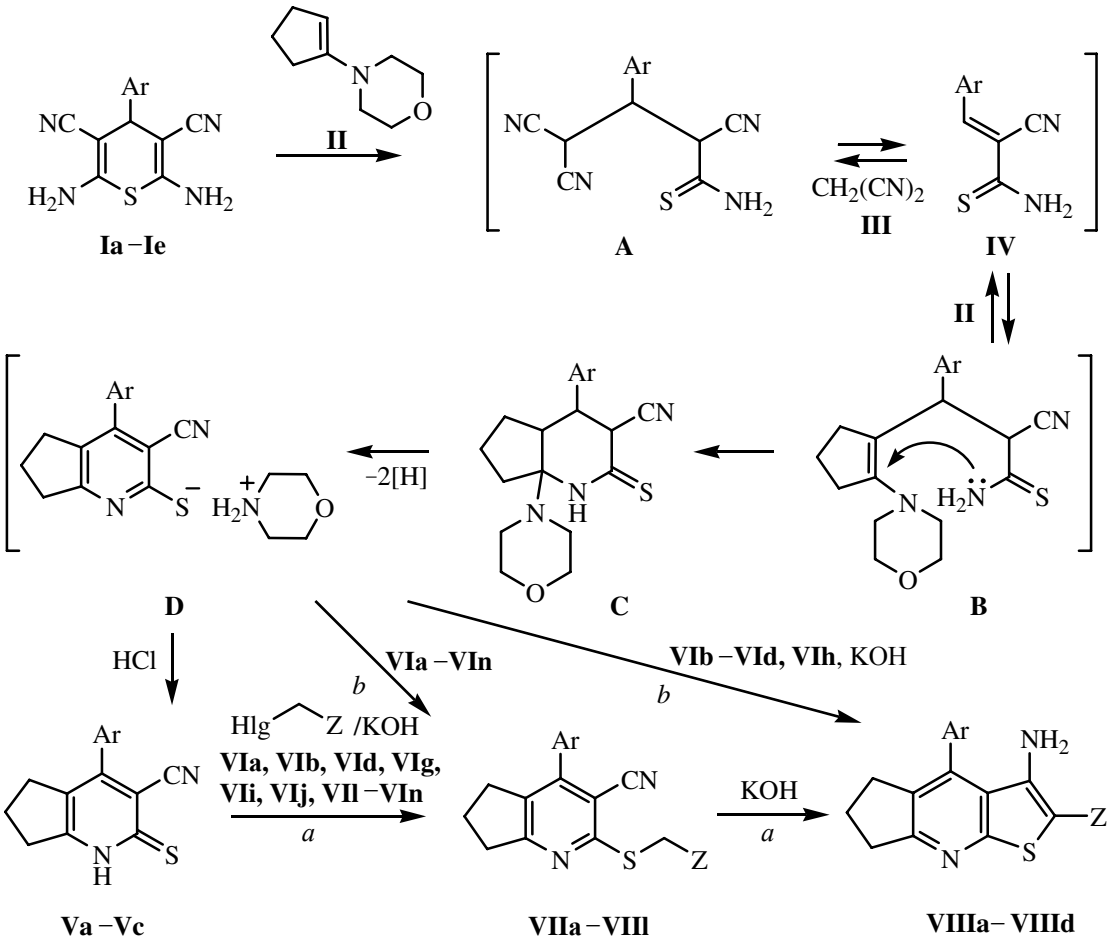
The interest of researchers to pyrindine derivatives is aroused by discovery among them of compounds with antiphlogistic [1], antidepressant [2], anticonvulsant [3], and antibacterial activity [4]. The main synthetic procedures for the pyrindine skeleton consist in the condensation of sodium salts of 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-dibenzyldicyclopentanone with cyanothioacetamide [7], reaction of cyclohexylidenecyanothioacetamide 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 β-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, VId, VIg, VIi, VIj**, and **VIl–VIn** 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–VIn** and a water solution of KOH (method *b*).

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



I, V, Ar=Ph (**a**), 4-ClC_6H_4 (**b**), 4-BrC_6H_4 (**c**), 4-$NO_2C_6H_4$ (**d**), 4-$Me_2CHC_6H_4$ (**e**); **VI**, Hlg=Cl (**a–i**), Br (**l–m**), I (**n**); Z=CO_2CHMe_2 (**a**), CONHPh (**b**), CN (**c**), CO_2Me (**d**), CO_2CH_2Ph (**e**), CO_2Ph (**f**), $CONH_2$ (**g**), 4-$MeOC_6H_4NHCO$ (**h**), CO_2Et (**i**), 4-ClC_6H_4CO (**j**), 2,4,5-$Me_3C_6H_2CO$ (**k**), COPh (l), $CH=CH_2$ (**m**), H (**n**); **VII**, Ar=Ph (**a**), 4-$Me_2CHC_6H_4$ (**b–e**), 4-ClC_6H_4 (**f–i**), 4-$NO_2C_6H_4$ (**j**), 4-BrC_6H_4 (**k, l**); Z=CO_2CHMe_2 (**a**), CONHPh (**b**), 4-ClC_6H_4CO (**c**), CO_2Et (**d**), H (**e**), COPh (**f**), $CH=CH_2$ (**g**), CO_2Me (**h**), $CONH_2$ (**i**), 2,4,5-$Me_3C_6H_2CO$ (**j**), CO_2Ph (**k**), CO_2CH_2Ph (**l**); **VIII**, Ar=4-$Me_2CHC_6H_4$ (**a, d**), 4-ClC_6H_4 (**b, c**); Z=CONHPh (**a**), CO_2Me (**b**), 4-$MeOC_6H_4NHCO$ (**c**), CN (**d**).

vibrations of amino group at 3195–3422 and 1640–1649 cm^{-1} respectively. In the ^1H 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_2 group appeared as a singlet in the region δ 3.95–4.88 ppm. At the same time the signals of SCH_2 group protons disappear from the spectra of compounds **VIIIa–VIIId**, and a signal of amino group protons is present instead at δ 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. ^1H NMR spectra were registered on spectrometers Bruker WP-100SY (100 MHz) (compounds **VIIk** and **VIII**), Gemini-200 (199.975 MHz) (compound **VIIa**), Varian Mercury-400 (400.397 MHz) (compounds **Ie** and **VIIj**), and Bruker DR-500 (500.13 MHz) (compounds **Vc**, **VIIb–VIIi**, and **VIIIa–VIIId**) from solutions in DMSO-d_6 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 1.95g (81%), white powder, mp 236–239°C (EtOH). IR spectrum, ν, cm^{-1}: 3465, 3327, 3190 (NH_2), 2200 sh (C≡N), 1650 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 1.24 d (6H, 2Me, *J* 7.12 Hz), 2.26 m (1H, C<u>H</u>Me_2), 4.15 s (1H, H^4), 6.54 br.s (4H, $2NH_2$), 7.16 d and 7.22 d (2H each, C_6H_4, *J* 7.13 Hz). Found, %: C 64.69; H 5.28; N 18.75. $C_{16}H_{16}N_4S$. Calculated, %: C 64.84; H 5.44; N 18.90.

4-Aryl-2-thioxo-2,5,6,7-tetrahydro-1*H*-[1]pyrindine-3-carbonitriles Va–Vc. A mixture of 10 mmol of an appropriate 4*H*-thiopyran **Ia–Ic** and 1.53 g (10mmol) 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]pyrindine-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]pyrindine-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]pyrindine-3-carbonitrile (Vc). Yield 1.59 g (54%), yellow powder, mp 228–230°C (AcOH). IR spectrum, ν, cm^{-1}: 2216 (C≡N). ^{1}H NMR spectrum, δ, ppm: 1.29 d (6H, 2Me, *J* 6.94 Hz), 2.03 m (2H, C^6H_2), 2.63 t (2H, C^7H_2, *J* 7.40 Hz), 3.03 t (2H, C^5H_2, *J* 4.60 Hz), 7.36 s (4H, C_6H_4), 14.21 br.s (1H, NH). Found,%: C 73.29; H 6.01; N 9.38. $C_{18}H_{18}N_2S$. Calculated,%: C 73.43; H 6.16; N 9.52.

4-Aryl-2-Z-methylsulfanyl-6,7-dihydro-5*H*-[1]-pyrindine-3-carbonitriles VIIa–VIIi. *a*. To a stirred solution of 10 mmol of an appropriate 2-thioxopyrindine **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, VId, VIg, VIi, VIj**, or **VIl–VIn**, 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-Isopropyloxycarbonylmethylsulfanyl-4-phenyl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIa). Yield 2.78 g (79%), yellow wool, mp 147°C (*i*-PrOH). IR spectrum, ν, cm^{-1}: 2218 (C≡N), 1735 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.26 d (6H, 2Me, *J* 6.30 Hz), 2.09 m (2H, C^6H_2), 2.83 t (2H, C^5H_2, *J* 7.24 Hz), 3.02 t (2H, C^7H_2, *J* 7.89 Hz), 3.99 s (2H, SCH_2), 4.95 m (1H, C<u>H</u>Me_2), 7.41–7.62 m (5H, Ph). Found,%: C 67.95; H 5.61; N 7.82. $C_{20}H_{20}N_2O_2S$. Calculated,%: C 68.16; H 5.72; N 7.95.

4-(4-Isopropylphenyl)-2-phenylcarbamoylmethylsulfanyl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIb). Yield 2.99 g (70%), yellow powder, mp 164–165°C (AcOH). IR spectrum, ν, cm^{-1}: 2217 (C≡N), 1672 (CONH). ^{1}H NMR spectrum, δ, ppm: 1.26 d (6H, 2Me, *J* 6.95 Hz), 2.07 m (2H, C^6H_2), 2.82 t (2H, C^5H_2, *J* 7.18 Hz), 2.99 m (3H, C^7H_2 and C<u>H</u>Me_2), 4.19 s (2H, SCH_2), 7.04 t (1H, Ph, *J* 6.97 Hz), 7.29 t (2H, Ph, *J* 6.97 Hz), 7.41 s (4H, C_6H_4), 7.58 d (2H, Ph, *J* 7.02 Hz), 10.16 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 427 (3)[*M*]$^+$, 335 (100) [*M* –PhNH]$^+$, 307 (34), 291 (15), 279 (10), 265 (61), 190 (11), 106 (15), 93 (38) [$PhNH_2$]$^+$, 77 (26) [Ph]$^+$, 65 (22), 43 (15). Found,%: C 72.89; H 5.70; N 9.67. $C_{26}H_{25}N_3OS$. Calculated,%: C 73.04; H 5.89; N 9.83. *M* 427.

4-(4-Isopropylphenyl)-2-(4-chlorobenzoylmethylsulfanyl)-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIc). Yield 2.46 g (55%), yellow powder, mp 123–124°C (ACOH). IR spectrum, ν, cm^{-1}: 2215 (C≡N), 1692 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.29 d (6H, 2Me, *J* 6.92 Hz), 1.98 m (2H, C^6H_2), 2.77 m (4H, C^5H_2 and C^7H_2), 2.97 m (1H, C<u>H</u>Me_2), 4.81 s (2H, SCH_2), 7.40 s (4H, C_6H_4), 7.61 d and 8.15 d (ïO 2H, 4-Cl_6H_4, *J* 8.57 Hz). Mass spectrum, *m/z* (I_{rel}, %): 448 (4) [*M* + 1]$^+$, 447 (5) [*M*]$^+$, 446 (8)[*M* – 1]$^+$, 445 (6) [*M* – 2]$^+$, 307 (84), 265 (26), 139 (100), 111 (32), 75 (9), 43 (5). Found,%: C 69.72; H 5.04; N 6.12. $C_{26}H_{23}ClN_2OS$. Calculated,%: C 69.86; H 5.19; N 6.27. *M* 447.

4-(4-Isopropylphenyl)-2-ethoxycarbonylmethylsulfanyl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIId). Yield 2.09 g (57%), white powder, mp 97–98°C (EtOH). IR spectrum, ν, cm^{-1}: 2219 (C≡N), 1732 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.28 t (3H, C<u>H</u>$_3$$CH_2$, *J* 6.16 Hz), 1.31 d (6H, 2Me, *J* 6.91 Hz), 2.07 m (2H, C^6H_2), 2.83 t (2H, C^5H_2, *J* 7.14 Hz), 3.02 m (3H, C^7H_2 and C<u>H</u>Me_2), 4.09 s (2H, SCH_2), 4.15 q (2H, OCH_2, *J* 6.16 Hz), 7.42 s (4H, C_6H_4). Found,%: C 69.28; H 6.11; N 7.18. $C_{22}H_{24}N_2O_2S$. Calculated,%: C 69.44; H 6.36; N 7.36.

4-(4-Isopropylphenyl)-2-methylsulfanyl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIe). Yield 2.03 g (66%), yellow powder, mp 95°C (EtOH). IR spectrum, ν, cm^{-1}: 2219 (C≡N). ^{1}H NMR spectrum, δ, ppm: 1.28 d (6H, 2Me, *J* 6.84 Hz), 2.07 m (2H, C^{6}H$_2$), 2.61 s (3H, SMe), 2.82 t (2H, C^{5}H$_2$, *J* 7.17 Hz), 2.99 m (1H, CHMe$_2$), 3.05 t (2H, C^{7}H$_2$, *J* 7.22 Hz), 7.40 s (4H, C$_6$H$_4$). Mass spectrum, *m/z* (I_{rel}, %): 310 (4)[*M* + 2]$^+$, 309 (13) [*M* + 1]$^+$, 308 (46) [*M*]$^+$, 307 (100) [*M* – 1]$^+$, 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. C$_{19}$H$_{20}$N$_2$S. Calculated,%: C 73.99; H 6.54; N 9.08. *M* 308.

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

2-Allylsulfanyl-4-(4-chlorophenyl)-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIg). Yield 2.02 g (62%), yellow powder, mp 99–100°C (MeOH). IR spectrum, ν, cm^{-1}: 2219 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.07 m (2H, C^{6}H$_2$), 2.80 t (2H, C^{5}H$_2$, *J* 7.25 Hz), 3.06 t (2H, C^{7}H$_2$, *J* 7.61 Hz), 3.95 d (2H, SCH$_2$, *J* 6.55 Hz), 5.14 d (1H, =CH$_2$, J_{cis} 9.56 Hz), 5.35 d (1H, =CH$_2$, J_{trans} 17.38 Hz), 5.96 m (1H, CH=), 7.50 d and 7.58 d (2H each, C$_6$H$_4$). Mass spectrum, *m/z* (I_{rel}, %): 329 (8) [*M* + 2]$^+$, 328 (31) [*M* + 1]$^+$, 327 (46) [*M*]$^+$, 326 (84) [*M* – 1]$^+$, 325 (87) [*M* – 2]$^+$, 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. C$_{18}$H$_{15}$ClN$_2$S. Calculated,%: C 66.15; H 4.63; N 8.57. *M* 327.

2-Methoxycarbonylmethylsulfanyl-4-(4-chlorophenyl)-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIh). Yield 2.43 g (68%), white powder, mp 135–137°C (MeOH). IR spectrum, ν, cm^{-1}: 2218 (C≡N), 1730 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.08 m (2H, C^{6}H$_2$), 3.80 t (2H, C^{5}H$_2$, *J* 7.21 Hz), 3.02 t (2H, C^{7}H$_2$, *J* 7.57 Hz), 3.68 s (3H, Me), 4.12 s (2H, SCH$_2$), 7.52 d and 7.59 d (ïO 2H, C$_6$H$_4$, *J* 8.47 Hz). Mass spectrum, *m/z* (I_{rel}, %): 360 (14)[*M* + 2]$^+$, 359 (28) [*M* + 1]$^+$, 358 (35) [*M*]$^+$, 357 (66) [*M* – 1]$^+$, 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. C$_{18}$H$_{15}$ClN$_2$O$_2$S. Calculated,%: C 60.25; H 4.21; N 7.81. *M* 359.

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

Compounds VIIa–VIIl. *b*. A mixture of 10 mmol of an appropriate 4*H*-thiopyran **Ia–Ie** and 1.53 g (10 mmol) of enamine **II** in 25ml 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–VIn**, 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-5*H*-[1]pyrindine-3-carbonitrile (VIIj). Yield 3.43 g (75%), yellow powder, mp 155–156°C (BuOH). IR spectrum, ν, cm^{-1}: 2220 (C≡N), 1688 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.09 m (2H, C^{6}H$_2$), 2.26 s (3H, Me), 2.30 s (3H, Me), 2.34 s (3H, Me), 2.59 t (2H, C^{5}H$_2$, *J* 7.19 Hz), 2.91 t (2H, C^{7}H$_2$, *J* 7.61 Hz), 4.62 s (2H, SCH$_2$), 7.00 s (1H$_{arom}$), 7.68 s (1H$_{arom}$), 7.75 d and 8.38 d (2H each, C$_6$H$_4$, *J* 6.99 Hz). Found,%: C 68.11; H 4.92; N 8.98. C$_{26}$H$_{23}$N$_3$O$_3$S. Calculated,%: C 68.25; H 5.07; N 9.18.

4-(4-Bromophenyl)-2-phenoxycarbonylmethylsulfanyl-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIk). Yield 2.56 g (55%), white powder, mp 190–192°C (ACOH). IR spectrum, ν, cm^{-1}: 2212 (C≡N), 1733 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.82 m (2H, C^{6}H$_2$), 2.85–3.16 m (4H, C^{5}H$_2$ and C^{7}H$_2$), 4.49 s (2H, SCH$_2$), 7.02–7.41 m (4H$_{arom}$), 7.52–7.64 m (3H$_{arom}$),

7.80 d ($2H_{arom}$, *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-Benzyloxycarbonylmethylsulfanyl-4-(4-bromophenyl)-6,7-dihydro-5*H*-[1]pyrindine-3-carbonitrile (VIIl). Yield 3.26 g (68%), yellow wool, mp 185–187°C (ACOH). IR spectrum, ν, cm^{-1}: 2220 (C≡N), 1729 (C=O). ^1H NMR spectrum, δ, 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 ($7H_{arom}$), 7.79 d ($2H_{arom}$, *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-5*H*-cyclopenta-[*b*]thieno[3,2-*e*]pyridines VIIIa and VIIIb *a*. To a stirred solution of 10 mmol of an appropriate thioether **VIIb** or **VIIh** in 15 ml of DMFwas 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-5*H*-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, ν, cm^{-1}: 3412, 3333, 3214 (NH_2), 1682 (CONH), 1645 [δ(NH_2)]. ^1H NMR spectrum, δ, 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, $C\underline{H}Me_2$), 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_{rel}, %): 429 (5)[*M* + 2]$^+$, 428 (16) [*M* + 1]$^+$, 427 (47) [*M*]$^+$, 335 (100) [*M* – PhNH]$^+$, 264 (38), 119 (10), 93 (18) [$PhNH_2$]$^+$, 77 (6) [Ph]$^+$, 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-5*H*-cyclopenta[*b*]thieno[3,2-*e*]pyridine-2-carboxamide (VIIIb). Yield 2.54 g (71%), yellow powder, mp 235–236°C (BuOH). IR spectrum, ν, cm^{-1}: 3422, 3312, 3195 (NH_2), 1731 (C=O), 1648 [δ(NH_2)]. ^1H NMR spectrum, δ, 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_{rel}, %): 360 (41)[*M* + 2]$^+$, 359 (23) [*M* + 1]$^+$, 358 (100) [*M*]$^+$, 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 **VIb–VId, VIh**, 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-5*H*-cyclopenta[*b*]thieno-[3,2-*e*]pyridine-2-carboxamide (VIIIc). Yield 3.05 g (68%), yellow powder, mp 235–237°C (ACOH). IR spectrum, ν, cm^{-1}: 3405, 3330, 3211 (NH_2), 1684 (CONH), 1640 [δ(NH_2)]. ^1H NMR spectrum, δ, 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-$MeOC_6H_4$, *J* 8.82 Hz), 7.42 d and 7.61 d (2H, 4-ClC_6H_4, *J* 8.53 Hz), 9.19 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 450 (5)[*M* + 1]$^+$, 449 (18) [*M*]$^+$, 327 (68), 297 (7), 264 (39), 123 (100) [4-$MeOC_6H_4NH_2$]$^+$, 108 (10), 95 (8), 77 (4) [Ph]$^+$. 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-5*H*-cyclopenta[*b*]thieno[3,2-*e*]pyridine-2-carbonitrile (VIIId). Yield 1.70 g (57%), yellow powder, mp 201–203°C (ACOH). IR spectrum, ν, cm^{-1}: 3403, 3311, 3199 (NH_2), 2214 (C≡N), 1649 [δ(NH_2)]. ^1H NMR spectrum, δ, 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, $C\underline{H}Me_2$), 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_{rel}, %): 335 (8)[*M* + 2]$^+$, 334 (25) [*M* + 1]$^+$, 333 (100) [*M*]$^+$, 332 (4) [*M* – 1]$^+$, 318 (15), 290 (21), 159 (22), 77 (6) [Ph]$^+$, 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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