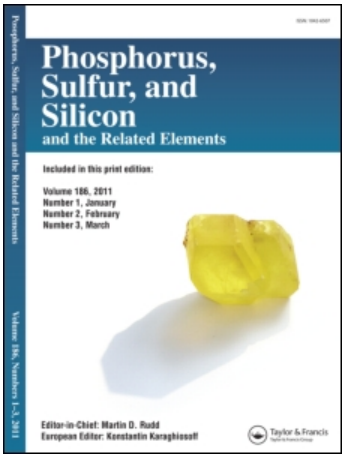

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SYNTHESIS OF PYRIDOTHIENOPYRIDINES AND ARYLAZOTHIENOPYRIDINES

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*Treatment of aminothienopyridine **3** with arylidenemalononitrile afford pyridothienopyridine **4**. Also condensation of **3** with ethyl ethoxymethylene-cyanoacetae afford compound **5**, which was cyclized in diphenyl ether into pyridothienopyridine **6**. Thiourea derivative **7** was cyclized using Br_2/AcOH, and ethyl chloroacetate to afford thiazolothienopyridine **8** and thiazolidinylthienopyridine **9** respectively. Compound **15** was condensed with aromatic aldehydes to give the corresponding arylidenethienopyridines **16a–d**. The latter compounds were underwent Michael addition with malononitrile to produce pyranothienopyridines **17a–d**. Compound **15** was coupled with aromatic diazonium chloride to give the corresponding 2-arylazothienopyridine derivatives **20**, but when treated with nitrous acis it dimerised into compound **19**.*

Thieno[2,3-b]pyridines are useful for multiple pharmacological applications. Thus, dihydrothieno[2,3-b]pyridine show remarkable effects as calcium antagonists[1] and also have been used in the treatment of epilepsy, Alzheimer's disease, and Huntington's chorea.[2] In continuation of our program in the synthesis of heterocycles compounds containing thieno[2,3-b] pyridine moiety,[3–10] we reported herein the synthesis of some new thienopyridine derivatives with hope that have potential biological activies.

Thus 3-amino-4,6-dimethylthieno[2,3-b]pyridine **3** allowed to react with arylidene malononitrile afforded the 2-amino-4-aryl-7,9-dimethyl-1,4-dihydropyrido[2′,3′:4,5]thieno[2,3-b]pyridine-3-carbonitrile (**4a–c**). The aminothienopyridine **3** upon reaction with ethyl ethoxymethylene-cyanoacetate gave compound **5**. The latter compound was cyclized in boiling diphenyl ether into 7,9-Dimethyl-4-oxo-1,4-dihydropyrido[2′,3′:

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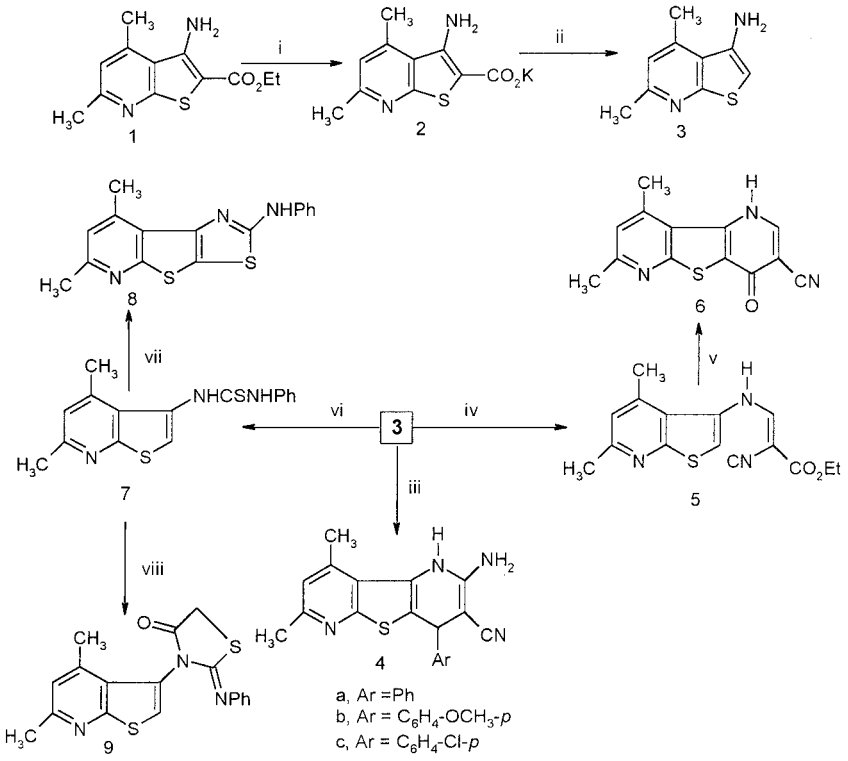
4,5]thieno[2,3-b]pyridine-3-carbonitrile (6). On the other hand, the compound **3** was reacted with phenyl isothiocyanate gave the corresponding thiourea derivative **7**. The latter compound underwent readily cyclization when treated with bromine in acetic acid solution to give **8**. Treatment of thiourea derivative **7** with ethyl chloroacetate in the presence of sodium acetate solution afforded thiazoledinylthienopyridine **9** (Scheme 1).

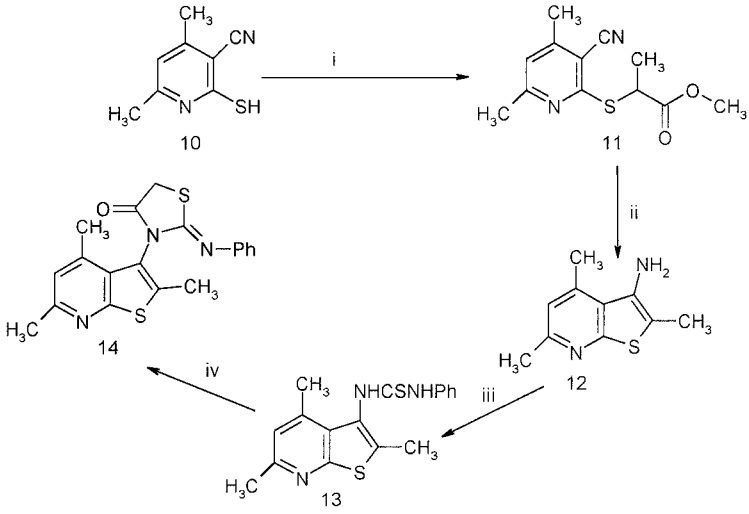


Reagents: i, KOH/EtOH; ii, EtOH/AcOH; iii, $ArCH{=}C(CN)_2$/EtOH/piperidine; iv, $EtOCH{=}C(CN)CO_2Et$; v, Diphenyl ether; vi, $PhNCS/C_6H_6$; vii. Br_2/AcOH: viii. $ClCH_2CO_2Et$/AcONa/EtOH

SCHEME 1

On the other hand, the treatment of 4,6-dimethyl-2-mercaptopyridine-3-carbonitrile (**10**) with methyl 2-bromo-propionate gave compound **11**. When the latter compound boiled with methanolic solution of sodium methoxide underwent cyclization accompanied with elimination of carboxylate group affording compound **12**. Treatment amino

compound **12** with phenyl isothiocyanate in benzene at reflux afforded the corresponding thiourea derivative **13** which undergoes cylization into thiazolidinone derivative **14** when treated with ethyl chloroacetate, furnish the corresponding thienopyridin-3-one **15**[11] (Scheme 2).

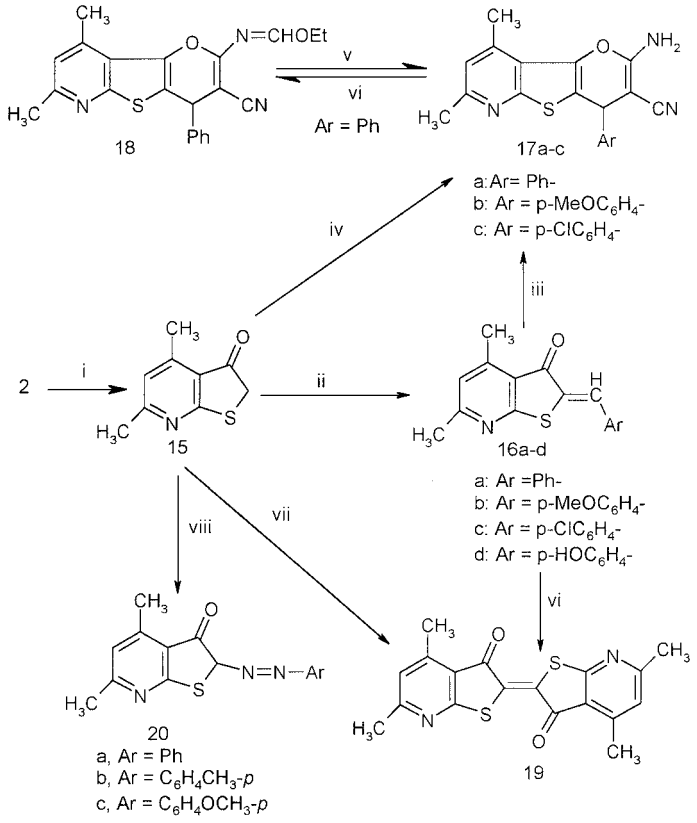


Reagents: $Br(CH_3)CHCO_2CH_3/CH_3CO_2Na/CH_3OH$; ii, CH_3ONa/CH_3OH; iii, $PhNCS/C_6H_6$; iv, $ClCH_2CO_2C_2H_5/C_2H_5OH/CH_3CO_2Na$

SCHEME 2

Condensation of latter compound with aromatic aldehydes in refluxing ethanol in the presence of catalytic amount of piperidine yield corresponding 2-arylidenethienopyridine-3-one derivatives **16a–d**. The latter compound was reacted with malononitrile in refluxing ethanol in the presence of triethyl amine to afford pyranothienopyridine (**17**). Compound **17a–c** also was obtained by an alternative route via treatment of **15** with arylidenemalononitrile in refluxing ethanol and in the presence of triethyl amine. Pyrano compound **17a** was reacted with triethyl orthoformate in the presence of acetic anhydride to give the corresponding ethoxymethylene amino derivative **18**, which when treated with amines or hydrazine hydrate underwent C=N bond fission to produce compound **17**. Attempt to synthesize 2-nitrozothieno-pyridin-3-one by its reaction with nitrous acid lead to the formation of dimer **19** instead of nitrozo compound. Also the dimmer compound **19** was produced when we try to react α-β-unsaturated compound **16** with hydrazines to synthesize pyrazolo compound, instead of the reaction of hydrazines with ketonic

group following with the addition into the double bond, it attacks the double bond to form compound **15** again, followed by its dimerization. The active methylene in compound **15** underwent coupling with aryl diazinum chloride to give 2-arylazoderivatives **20** (Scheme 3).



Reagents: i, orthophosphoric acid; ii, ArCHO/EtOH/piperidine; iii, $CH_2(CN)_2$/EtOH/piperidine; iv, $ArCH{=}C(CN)_2$/EtOH/piperidine v, $CH(OEt)_3/Ac_2O$; vi, $PHNHNH_2$ or NH_2NH_2; vii, $NaNO_2$/HCl; viii, $ArN{=}NCl/EtOH/CH_3CO_2Na$

SCHEME 3

EXPERIMENTAL

All melting points were uncorrected and were determined on a Kofler melting point apparatus. The IR spectra were recorded on a

Pye-Unicam spectrometer using KBr Wafer technique. ^{1}HNMR spectra were recorded on a Varian 390 90 MHz NMR spectrometer using TMS as an internal standard. The chemical shift were expressed as δ, units ppm. Mass spectra were recorded in on JEOL JMS 600 spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 C microanalyzer. Compounds **1–3**,**15** were prepared by the following published procedure.[11]

General Procedure for the Synthesis of 4a—c

A mixture of compound **3** (1.76 g, 0.01 mmol) and aryledinemalononitrile (0.01 mmol) in ethanol (30 ml), few drops of piperidine were added. The mixture was heated under reflux for 3 h. The solid product so formed on heating was collected and recrystallized from DMF as yellow crystals.

2-Amino-1,4-dihydro-7,9-dimethyl-4-phenylpyrido[2′,3′: 4,5]thieno[2,3-b]pyridine-3-carbonitrile (4a)

Produced 78% yield, m.p. 298–300°C. IR: $\nu = 3400$ cm^{-1} (NH), 3200,3100 cm^{-1} (NH_2) and 2220 cm^{-1} (CN). ^{1}HNMR (DMSO-d_6): $\delta = 2.4$, 2.7 (2s, 6H, $2CH_3$), 5.6 (s, 1H, CH-dihydropyridine), 6.5(s, 2H, NH_2), 6.9 (s, H, CH-pyridine), 7.3–7.8 (m, 5H, ArH) and 11.3 (s, 1H, NH). MS; EI: m/z = 332 (M^+).

Anal. Calcd. for $C_{19}H_{16}N_4S$(332.42): C, 68.65; H, 4.85; N, 16.85; S, 9.65%.; Found: C, 68.44; H, 4.83; 17.00; 9.37.

2-Amino-1,4-dihydro-7,9-dimethyl-4-(p-methoxyphenyl)-pyrido[2′,3′:4,5]thieno-[2,3-b]pyridine-3-carbonitrile (4b)

Produced in 74% yield; m.p. 238–340°C; IR: ν = 3420, 3320 cm^{-1} (NH_2), 3170 cm^{-1} (NH) and at 2220 cm^{-1} (CN). ^{1}HNMR (DMSO-d6): $\delta = 2,4$, 2.7(2s, 6H, $2CH_3$), 3.6(s, 3H, OCH_3), 5.2(s, 1H, CH- dihydropyridine), 6.3 (s, 2H, NH_2), 6.9 (s, 1H, CH-pyridine), 7.4, 7.9 (2dd, 4H, Ar—H), 9.5 (s, 1H, NH).

Anal. Calcd. for $C_{20}H_{18}N_4OS$(362.12): C, 66.28; H, 5.01; N, 15.46; S, 8.85%; Found: C, 66.04; H, 5.28; N, 15.66; S, 9.07.

2-Amino-4-(p-chlorophenyl)-1,4-dihydro-7,9-dimethyl-pyrido[2′,3′:4,5]thieno-[2,3-b]pyridine-3-carbonitrile (4c)

Produced in 82% yield, m.p. 220–222°C; IR: $\nu = 3500$ cm^{-1} (NH), 3300, 3200 cm^{-1} (NH_2) and 2210 cm^{-1} (CN). ^{1}HNMR (DMSO-d_6): $\delta = 2.4$, 2.7 (2s, 6H, $2CH_3$), 5.4(s, 1H, CH-dihydropyridine), 6.1 (s, 2H, NH_2), 6.9 (s, 1H, CH-pyridine), 7.1, 7.6 (2d, 4H, Ar—H), 10.5 (s, 1H, NH).

Anal. Calcd. For $C_{19}H_{15}ClN_4S$(366.87): C, 62.20; H, 4.12; N, 15.27; S, 8.74; Cl, 9.66; Found: C, 62.42; H, 4.12; N, 15.17; S, 8.88; Cl, 9.85.

Ethyl 2-Cyano-3[4,6-dimethylthieno[2,3-b]pyridine-3-yl]aminoacrylate (5)

A mixture of compound **3** (1.76 g, 0.01 mmol) and ethoxymethylene ethyl cyanoacetate (1.70 g, 0.01 mmol) in ethanol (20 ml) and few drops of acetic acid was added. The mixture was heated under reflux for 2 h, then allowed to cool. The solid product was collected by filtration and recrystallized from ethanol as yellowish white crystals in 78% yield, m. p. 220–222°C; IR: 3200 cm^{-1} (NH), 2210 (CN) and 1700 cm^{-1} (C=O). ^{1}HNMR ($CDCl_3$): 1.4 (t, 3H, CH_3), 2.6, 2.85 (2s, 6H, $2CH_3$), 4.35 (q, 2H, CH_2), 7.00 (s, 1H, CH-pyridine), 7.25(s, 1H, CH thiophene), 7.95(d, 1H, CH=N) and 11.25 (d, 1H, NH).

Anal. Calcd. for $C_{15}H_{15}N_3O_2S$(301.36): C, 59.78; H, 5.02; N, 13.94; S, 10.64; Found: C, 60.02; H, 4.82; N, 14.08; S, 10.52.

7,9-Dimethyl-4-oxo-1,4-dihydropyrido[2′,3′:4,5]thieno[2,3-b]pyridine-3-carbonitrile (6)

A solution of **5** (1.5 g, 0.005 mmol) in diphenyl ether (10 ml) was heated under reflux for 3 h, then allowed to cool. The solid product which precipitated was collected by filtration and recrystallized from dioxan as yellow crystals in 45% yield, m.p 310–312°C; IR: $\nu = 3150$ cm^{-1} (NH), 2220 cm^{-1} (CN), 1700 cm^{-1} (C=O). ^{1}HNMR(DMSO-d_6): $\delta = 2.3$, 2.7 (2s, 6H, $2CH_3$), 6.9, 7.3 (2s, 2H, CH-pyridine), and at 10.5 (s, 1H, NH). MS; EI: m/z = 243(M^+).

Anal. Cal. for $C_{13}H_9N_3OS$(243.28): C, 61.16; H, 3.55; N, 16.46; S, 12.56; Found: C, 61.04; H, 3.82; N, 16.67; S, 12.30.

N-(4,6-Dimethylthieno[2,3-b]pyridin-3-yl)-N′-phenylthiourea (7)

A mixture of amino compound **3** (0.01 mmol) and phenyl isothiocyanate (0.01 mmol) in benzene (30 ml) was heated under reflux for 2 h, then allowed to cool. The solid product was collected and recrystallized from ethanol as white crystals in 76% yield, m.p. 201–203°C; IR: $\nu = 3450$, 3250 cm^{-1} (2NH), 2950 cm^{-1} (CH-aliphatic) and 1500 cm^{-1} (C=S). ^{1}HNMR (DMSO-d_6): $\delta = 2.4$,2.6 (2s, 6H, $2CH_3$), 6.7 (s, 1H, CH-thiophene), 6.9 (s, 1H, CH-pyridine), 7.3–7.6 (m, 5H, Ar H), 9.8, and 11.4 (2s, 2H, 2NH).

Anal. Calcd for $C_{16}H_{15}N_3S_2$(313.44): C, 61.31; H, 4.82; N, 13.41; S, 20.46; Found: C, 61.12; H, 5.00; N, 13.53; S, 20.32.

2,4-Dimethyl-6-phenylaminothiazolo[4′,5′:4,5]thieno-[2,3-b]pyridine (8)

To solution of thiourea derivative **7** (0.01 mmol) in acetic acid 30 ml, bromine (0.01 mmol) in acetic acid (10 ml) was added dropwise with stirring during 15 min. The stirring was continued for additional 1 h and then (100 ml) water was added. The solid product was collected, washed well with water and recrystallized from ethanol as yellowish white crystals in 72% yield, m.p 199–200°C. IR: $\nu = 3300$ cm^{-1} (NH); ^{1}HNMR (DMSO-d_6): $\delta = 2.4$, 2,6 (2s, 6H, $2CH_3$), 6.9 (s, 1H, CH-pyridine), 7–7.6 (m, 5H, Ar—H), and 11.3 (s, 1H, NH). MS; EI: m/z = 311(M^+).

Anal. Calcd for $C_{16}H_{13}N_3S_2$(311.42): C, 61.73; H, 4.21; N, 13.51; S, 20.56; Found: C, 61.98; H, 4.06; N, 13.65; S, 20.76.

3-(4,6-Dimethyl-thieno[2,3-b]pyridine-3-yl)-2-phenylimino-thiazolidin-4-one (9)

A mixture of compound **7** (3.13 g, 0.01 mmol), ethyl chloroacetate (1.22 g, 0.01 mmol), and sodium acetate (0.012 mmol) in ethanol (30 ml) was heated under ereflux for 4 h, then allowed to cool, poured into cold water (100 ml). The solid product was collected and recrystallized from ethanol as white crystals in 69% yield, m.p. 188–190°C; IR: $\nu = 1680$ cm^{-1} (C=O) and 1600 cm^{-1} (C=N). ^{1}HNMR ($CDCl_3$): $\delta = 2.3$, 2,6 (2s, 6H, $2CH_3$), 4.1 (s, 2H, CH_2), 6.9 (s, 1H, CH-pyridine), 7.3–7.8 (m, 5H, Ar—H.

Anal. Calcd. for $C_{18}H_{15}N_3OS_2$(353.46): C, 61.17; H, 4.28; N, 11.89; S, 18.14; Found: C, 60.99; H, 4.52; N, 12.08; S, 18.00.

Methyl 2-(3-Cyano-4,6-dimethylpyridin-2-yl)mercapto-2-methylacetate (11)

A mixture of compound **10** (1.64 g, 0.01 mmol), methyl 2-bromopropionate (1.67 g, 0.01 mmol), and sodium acetate (0.012 mmol) in methanol (30 ml) was refluxed for 2 h, then allowed to cool, and poured into water. The solid product so formed was collected by filtration, recrystallized from a mixture of methanol/water (1:1) in 78% yield, m.p. 64–66°C; IR: $\nu = 2220$ cm^{-1} (CN), and 1710 cm^{-1} (C=O). ^{1}HNMR ($CDCl_3$): $\delta = 1.5$ (d, 3H, CH_3), 2.3 (s, 6H, $2CH_3$), 3.3 (s 3H, CH_3). 4.2–4.5 (q, 1H, CH) and 6.8 (s, 1H, CH-pyridine).

Anal. Calcd. For $C_{12}H_{14}N_2O_2S$ (250.32): C , 57.58; H, 5.64; N, 11.19; S, 12.81; Found: C , 57.72; H, 5.83; N, 10.98; S, 13.04.

3-Amino-2,4,6-trimethylthieno[2,3-b]pyridine (12)

Method A

A sample of compound **11** (2 g) was boiled for 1 h in methanol (30 ml) containing sodium methoxide (0.02 mmol). The reaction mixture then allowed to cool and poured into cold water (70 ml). The solid product was filtered off and recrystallized from methanol as white crystals in 74% yield, m.p. 126–128°C.

Method B

A mixture of compound **10** (1.64 g, 0.01 mmol), methyl-β-bromopropionate (1.67 g, 0.01 mmol), and K_2CO_3 (0.02 mmol in methanol (30 ml) was refluxed for 4 h then allowed to cool. The solid product performed was collected by filtration, and recrystallized from methanol as white crystals, in 70% yield, m.p. 126–128°C; IR: $\nu = 3350$, 3250 cm^{-1} (NH_2). ^{1}HNMR ($CDCl_3$): $\delta = 2.2$, 2.5, 2.7 (3s, 9H, $3CH_3$), 3.2–3.5 (broad band, 2H, NH_2) and 6.8 (s, 1H, CH pyridine).

Anal. Calcd. For $C_{10}H_{12}N_2S$ (192.28): C, 62.47; H, 6.29; N, 14.57; S, 16.67; Found: C, 62.24; H, 6.08; N, 14.79; S, 16.84.

N-(2,4,6-Trimethylthieno[2,3-b]pyridin-3-yl)-N′-phenylthiourea (13)

A mixture of compound **12** (1.93 g, 0.01 mmol) and phenyl isothiocyanate (1.35 g, 0.01 mmol) in benzene (30 ml) was refluxed for 5 h, then allowed to cool. The solid product was collected and recrystallized from ethanol as white crystals in 78% yield, m.p. 210–212°C; IR: $\nu = 3450$ cm^{-1} and 3250 cm^{-1} (2NH). ^{1}HNMR($CDCl_3$): 2.2, 2.5, 2.7 (3s, 9H, $3CH_3$), 6.9 (s, 1H, CH pyridine), 7,2–7.7 (m, 5H, ArH); 9.6, 11.3 (2s, 2H, 2NH).

Anal. Calcd. for $C_{17}H_{17}N_3S_2$ (327.46): C, 62.35; H, 5.23; N, 12.83; S, 19.58 ; Found: C, 62.56; H, 5.00; N, 13.04; S, 19.72.

2-Phenylimino-3(2,4,6-Trimethyl-thieno[2,3-b]pyridin-3-yl]-thiazolidin-4-one (14)

A mixture of compound **13** (3.27 g, 0.01 mmol), ethyl chloroacetate (1.22 g, 0.01 mmol), and sodium acetate (0.012 mmol) in ethanol (30 ml) was heated under reflux for 5 h, then allowed to cool and poured into cold water (100 ml). The solid product was collected and recrystallized from ethanol as white crystals, in 67% yield, m.p. 227–230°C; ^{1}HNMR ($CDCl_3$): $\delta = 2.3$, 2.5, 2,8 (3s, 9H, $3CH_3$), 4.1 (s, 2H, CH_2), 6.9 (s, 1H, CH pyridine), 7.3–7.9 (m, 5H, ArH) and 8.3 (broad s, 1H, NH).

Anal. Calcd. For $C_{19}H_{17}N_3OS_2$ (367.49): C, 62.10; H, 4.66; N, 11.43; S, 17.45; Found: C, 62.12; H, 4.39; N, 11.18; S, 17.56.

General Procedure for the Synthesis of 16a–d

To a mixture of compound **15** (0.01 mmol) and aryl aldehyde (0.01 mmol) in ethanol (30 ml), and a few drops of piperidine were added. The mixture was heated under reflux for 2 h, then allowed to cool. The solid product was collected and recrystallized from dioxan.

2-Benzyledine-4,6-dimthyl-1,2-dihydrothieno[2,3-b]pyridin-3-one (16a)

Produced in 77% yield, m.p. 174–176°C; IR: $\nu = 3050$ cm^{-1} (CH-aromatic) and 1690 cm^{-1} cm^{-1}. ^{1}HNMR (DMSO-d_6): $\delta = 2.3$, 2.5 (2s, 6H, $2CH_3$), 6.7 (s, 1H, C=CH), 6.9 (s, 1H, CH-pyridine) and 7.3–7.6 (m, 5H, ArH).

Anal. Calcd. for $C_{16}H_{13}NOS$(267.35): C, 71.85; H, 4.90; N, 5.24; S, 11.99; Found: C, 71.63; H, 5.13; N, 5.53; S, 12.23.

4,6-Dimthyl-1,2-dihydro-2-(4-methoxybenzyledine)thieno-[2,3-b]pyridin-3-one (16b)

Produced in 85% yield, m.p. 182–184°C; IR: $\nu = 1690$ cm^{-1} (CO). ^{1}HNMR (DMSO-d_6): $\delta = 2.3$, 2.5 (2s, 6H, $2CH_3$), 3.2 (s, 3H, OCH_3), 6.9 (s, 1H, CH-pyridine) and 7.1,7.6 (2d, 4H, ArH), 7.8 (s, 1H, C=CH).

Anal. Calcd. for $C_{17}H_{15}NO2S$(297.37): C, 68.66; H, 5.08; N, 4.71; S, 10.78%. Found: C, 68.39; H, 4.87; N, 4.95; S, 11.00.

2-(4-Chlorobenzyledine)-4,6-dimthyl-1,2-dihydrothieno-[2,3-b]pyridin-3-one (16c)

Produced in 78% yield, m.p. 199–200°C; Lit.[13] m.p. 198°C.

4,6-Dimthyl-1,2-dihydro-2-(4-hydroxybenzyledine) thieno-[2,3-b]pyridin-3-one (16d)

Produced in 72% yield, m.p. > 300°C; IR: $\nu = 3450$ cm^{-1} (OH) and 1690 cm^{-1} (CO). ^{1}HNMR (DMSO-d_6): $\delta = 2.3$, 2.5 (2s. 6H, $2CH_3$), 6.9 (s, 1H, CH-pyridine) and 7.2, 7.8 (2d, 4H, ArH), 8.0 (s, 1H, C=CH) and 9.3 (s, 1H, OH).

Anal. Calcd. for $C_{16}H_{13}NO_2S$ (283.35): C, 67.82; H, 4.62; N, 4.94; S, 11.32. Found: C, 67. 98; H, 4.83; N, 5.17; S, 11.53.

General Procedure for the Synthesis of 17a–c

Method A

A mixture of **16** (0.01 mmol), malononitrile (0.01 mmol), and few drops of piperidine in ethanol (30 ml), was heated under reflux for 2 h, then allowed to cool. The solid product was collected and recrysalized from ethanol.

Method B

A mixture of compound **15** (0.01 mmol), arylidenemalononitrile (0.01 mmol), and few drops of triethyl amine as a catalyst in ethanol (30 ml) was refluxed for 3 h, then allowed to cool. The solid product was collected and recrystallized from ethanol.

2-Amino-7,9-dimethyl-4[H]-4-phenyl-pyrano[2′,3′:4,5]-thieno[2,3-b]pyridine-3-carbonitrile (17a)

Produced 78% yield, m.p. 265–268°C; IR: $\nu = 3340, 3230\ cm^{-1}$ (NH_2), $2210\ cm^{-1}$ (CN). ^{1}HNMR ($CDCl_3$): 3.4, 3.6 (2s, 6H, $2CH_3$), 4.7(s, 1H, CH-pyran), 6.5 (s, 2H, NH_2), 6.9 (s,1H,CH-pyridine), 7.0–7.4 (m, 5H, Ar—H).

Anal. Calcd. for $C_{19}H_{15}N_3OS$ (333.41): C, 68.45; H, 4.53; N, 12.60; S, 9.62. Found: C, 68.68; H, 4.77; N, 12.42; S, 9.78.

2-Amino-7,9-dimethyl-4[H]-4-[4-methoxyphenyl]pyrano-[2′,3′:4,5]thieno[2,3-b]pyridine-3-carbonitrile (17b)

Produced in 87% yield, m.p. 183–185°C; IR: $\nu = 3360, 3260\ cm^{-1}$ (NH_2), and at $2220\ cm^{-1}$ (CN). ^{1}HNMR (DMSO-d_6): $\delta = 2.3, 2.7$(2s, 9H, $3CH_3$), 3.6(s, 3H, OCH_3), 4.6 (s, 1H, CH-pyran), 6.9 (s, 1H, CH-pyridine) and at 7.0, 7.6 (2d, 4H, Ar—H).

Anal. Calcd. for $C_{20}H_{17}N_3O_2S$ (363.10): C, 66.10; H, 4.71; N, 11.56; S, 8.82. Found: C, 66.00; H, 5.00; N, 11.72; S, 9.00.

2-Amino-[4-chlorophenyl]-7,9-dimethyl-4[H]-pyrano[2′,3′:4,5]thieno[2,3-b]pyridine-3-carbonitrile (17c)

Produced in 82% yield, m.p. 288–290°C; IR: $\nu = 3380, 3280\ cm^{-1}$ (NH_2), and at $2220\ cm^{-1}$ (CN). ^{1}HNMR (DMSO-d_6): $\delta = 2.4$, 2.7 (2s, 6H, $2CH_3$), 4.7 (s, 1H, CH-pyran), 6.9 (s, 1H, CH-pyridine) and at 7.1, 7.6 (2d, 4H, Ar—H).

Anal. Calcd. for $C_{19}H_{14}ClN_3OS$ (367.85): C, 62.04; H, 3.84;Cl, 9.64; N, 11.42; S, 8.72. Found: C, 61.88; H, 4.07;Cl. 9.78; N, 11.32; S, 8.78.

2-Ethoxymethyleneamino-4-phenyl-4[H]7,9-dimethylpyrano[2′,3′:4,5]thieno[2,3-b]pyridine-3-carbonitrile (18)

A mixture of compound **17a** (3.33 g, 0.01 mmol) and triethyl orthoformate (0.02 mmol) in acetic anhydride (20 ml) was heated under reflux for 2 h, allowed to cool, and poured into (100 ml). The solid product was collected and recrystallized from ethanol as white crystals in 72% yield, m.p. 210–213°C; IR: 2220 cm^{-1} (CN). ^{1}HNMR ($CDCl_3$): $\delta = 1.4$–1.6 (t, 3H, CH_3), 2.5. 2.7 (2s, 6H, CH_3). 4.3–4.6 (q. 2H, CH_2), 4.95 (s, 1H, CH-pyran). 6.9 (s, 1H, CH-pyridine), 7.1–7,5 (m, 5H, Ar—H). and 8.2 (s, 1H, CH=N).

Anal. Calcd. For $C_{22}H_{19}N_3O_2S$ (389.47): C, 67.85; H, 4.92; N, 10.79; S, 8.23. Found: C, 68.05; H, 4.16; N, 10.52; S, 8.05.

4,6,4′,6′-Tetramethyl[2.2′]bi[thieno]2,3-b]pyridinylidene-3,3′-dione(19)

Method A

A mixture of compound **16a** (2.67 g, 0.01 mmol) and phenyl hydrazine (1.08 g, 1.0 mmol) in ethanol (30 ml) was heated under reflux for 3 h. The red crystals, which precipitated while heating, was filtered off while hot and identified as compound **19**. The filtrate was evaporated and the residue was identified as benzyledine phenyl hydrazone. m.p. lit.[12]

Method B

To a stirred solution of compound **15** (1.79 g, 0.01 mmol) in acetic acid (20 ml), sodium nitrite solution (0.02 mmol) in water (5 ml) was added dropwise over 10 min. The solid product was collected and recrystallized from dioxan in 78% yield and identified as compound **19**. Produced as red crystals in 65% yield, m.p. > 300°C; IR: $\nu = 1680$ cm^{-1} (C=O). ^{1}HNMR(CF_3COOD): 2.4. 2.6 (2s, 12H, $4CH_3$) and at 7.0 (s, 2H, 2CH-pyridine). MS; EI: m/z = 354(M^+).

Anal. Calcd for $C_{18}H_{14}N_2O_2S_2$ (354.44): C, 61.00; H, 3.98; N, 7.90; S, 18.09. Found: C, 60.78; H, 4.24; N, 8.13; S, 17.

2-Arylazo-4,6-dimthylthieno[2,3-b]pyridin-3-one (20)

To a solution of compound **15** (1.79 g, 0.01 mmol) in ethanol containing 0.05 mmol sodium acetate, a solution of diazotized aromatic amine (0.01 mmol) was added dropwise with stirring at 5°C over 16 min. After the addition was complete the stirring was continued for 1 h,

then allowed to stand for 2 h. The solid product was collected and recrystallized from ethanol.

4,6-Dimthyl-2-phenylazothieno[2,3-b]pyridin-3-one (20a)

Produced in 78% yield, m.p. 178°C; IR: 3350 cm^{-1} (NH). 1680 cm^{-1} (C=O). ^{1}HNMR($CDCl_3$); $\delta = 2.4$, 2.6 (2s, 6H, $2CH_3$), 6.9 (s, 1H, CH-pyridine), 7.1–7.6 (m, 5H, Ar–H), 11.2 (s, 1H, NH).

Anal. Calcd. for $C_{15}H_{13}N_3OS$ (283.35): C, 63.58; H, 4.62; N, 14.83; S, 11.31. Found: C, 63.75; H, 4.77; N, 15.05; S, 11.08.

4,6-Dimthyl-2-(4-methylphenyl)-azothieno[2,3-b]pyridin-3-one (20b)

Produced in 76% yield, m.p. 180°C; IR: 3350 cm^{-1} (NH). 1680 cm^{-1} (C=O). ^{1}HNMR ($CDCl_3$); $\delta = 2.2$, 2.4, 2.6 (3s, 9H, $3CH_3$), 6.9 (s, 1H, CH-pyridine), 7.0–7.6 (2d, 4H, Ar–H), 9.9, 13.2 (2s, 1H, NH–OH tautomer).

Anal. Calcd. for $C_{16}H_{15}N_3OS$ (297.37): C, 64.62; H, 5.08; N, 14.13; S, 10.78. Found: C, 64.88; H, 4.88; N, 13.84; S, 11.00.

4,6-Dimthyl-2-(4-methoxyphenyl)-azothieno[2,3-b]pyridin-3-one (20c)

Produced in 82% yield, m.p. 205°C; IR: 3350 cm^{-1} (NH). 1680 cm^{-1} (C=O).

Anal. Calcd. for $C_{16}H_{15}N_3O_2S$ (313.37): C, 61.32; H, 4.82; N, 13.41; S, 10.23. Found: C, 61.15; H, 5.05; N, 13.67; S, 10.04.

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