Synthesis of pyridothienopyridines and arylazothienopyridines

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Treatment of aminothienopyridine **3** with arylidenemalononitrile affords pyridothienopyridine **4**. Condensation of **3** with ethyl ethoxymethylene-cyanoacetate affords compound **5**, which may be cyclised in diphenyl ether into pyridothienopyridine **6**. Thiourea derivative **7** is cyclised using Br_2/ AcOH, and ethyl chloroacetate to afford thiazolothienopyridine **8** and thiazolidinylthienopyridine **9** respectively. Compound **15** is condensed with aromatic aldehydes to give the corresponding arylidenethienopyridines **16a–d**. The latter compounds undergo 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 acids it dimerised to compound **19**.

Keywords: synthesis, pyridothienopyridines and arylazothienopyridines

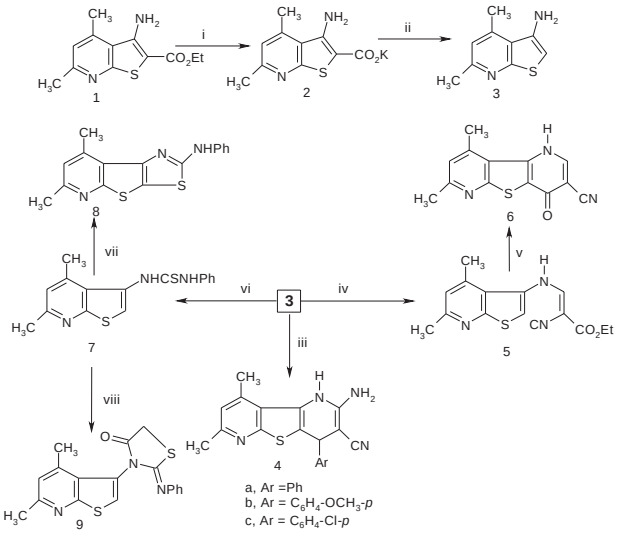
Thieno[2,3-b]pyridines have useful pharmacological applications. Thus, dihydrothieno[2,3-b]pyridine are calcium antagonists[1] and have been used in the treatment of epilepsy, Alzheimer's disease, and Huntington's chorea.[2] In continuation of our program in the synthesis of heterocycles compounds containing thieno[2,3-b]pyridine moiety,[3-10] we now report the synthesis of some new thienopyridine derivatives.

Results and discussion

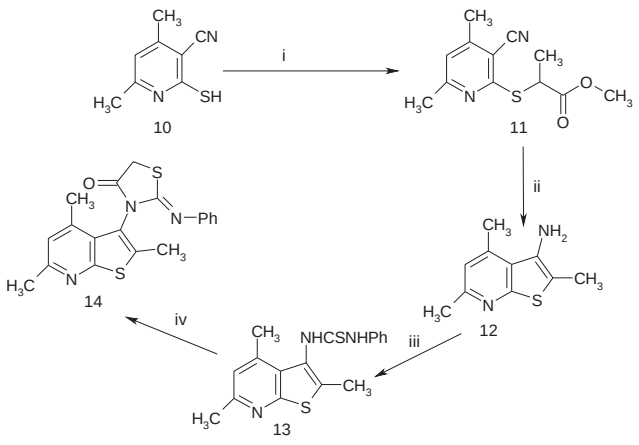
A 3-amino-4,6-dimethylthieno[2,3-b]pyridine **3**[11] reacts with arylidene malono-nitrile to give the 2-amino-4-aryl-7,9-dimethyl-1,4-dihydropyrido[2',3':4,5]thieno[2,3-b]pyridine-3-carbonitriles (**4a-c)**. A recent report by E. A. Bakhite[12] that 3-amino-4-(*p*-methoxyphenyl)-5,6,7,8-tetrahydrothieno[2,3-b]quinoline reacts with ethyl ethoxy-methylenecyanoacetate to afford 3(3-amino-4-(*p*-methoxyphenyl)-5,6,7,8-tetrahydro-thieno-[2,3-b]quinolin-2-yl)-2-cyano-acrylate led us to apply this reaction with compound **3** which gives compound **5**. The structure of compound **5** is confirmed by its ^{1}H NMR in $CDCl_3$ spectrum, while it gave signals 7.25(s, 1H, CH thiophene), 7.95(d, 1H, CH=N) and 11.25 (d, 1H, NH). These data indicate that the reaction occurred at the amino group instead of the CH of thiophene as reported before. This product cyclises in boiling diphenyl ether to 7,9-dimethyl-4-oxo-1, 4-dihydropyrido[2',3':4,5]thieno[2,3-b]pyridine-3-carbo-nitrile **(6)**. Compound **3** reacts with phenyl isothiocyanate to give the corresponding thiourea derivative **7**. The latter readily undergoes cyclisation when treated with bromine in acetic acid solution to give **8**. Treatment of the thiourea derivative **7** with ethyl chloroacetate in the presence of sodium acetate solution afforded thiazoledinylthienopyridine **9** (Scheme 1).

Treatment of 4,6-dimethyl-2-mercaptopyridine-3-carbonitrile (**10)** with methyl 2-bromopropionate gave compound **11**. When the latter is boiled with methanolic solution of sodium methoxide, it undergoes cyclisation accompanied with elimination of carboxylate group to give compound **12**. Treatment of the amino compound **12** with phenyl isothiocyanate in benzene under reflux affords the corresponding thiourea derivative **13** which undergoes cyclisation into thiazolidinone derivative **14** when treated with ethyl chloroacetate. (Scheme 2).

Treatment of compound **2** with orthophosphoric acid furnishes the corresponding thienopyridin-3-one **15**[11] Condensation of the latter with aromatic aldehydes in refluxing ethanol in the presence of a catalytic amount of piperidine yields the corresponding 2-arylidenethienopyridine-3-one derivatives **16a–d**. The latter react with malononitrile in refluxing ethanol in the presence of triethylamine to afford pyranothienopyridine (**17**). Compounds **17a–c** are also obtained by an alternative route via treatment of **15** with arylidenemalononitrile in refluxing ethanol in the presence of triethylamine. This pyran **17a** reacts with triethyl orthoformate in the presence of acetic anhydride to give the corresponding ethoxymethylene amino derivative **18**, which when treated



Scheme 1 Reagents: i, KOH/EtOH; ii, EtOH/AcOH; iii, $ArCH=C(CN)_2$/EtOH/piperidine; iv, $EtOCH=C(CN)CO_2$ Et; v, Diphenyl ether; vi, $PhNCS/C_6H_6$ vii, Br_2/AcOH; viii, $ClCH_2CO_2Et$/AcONa/EtOH.



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, $ClCH_2CO_2C_2H_5/C_2H_5OH/CH_3CO_2Na$.

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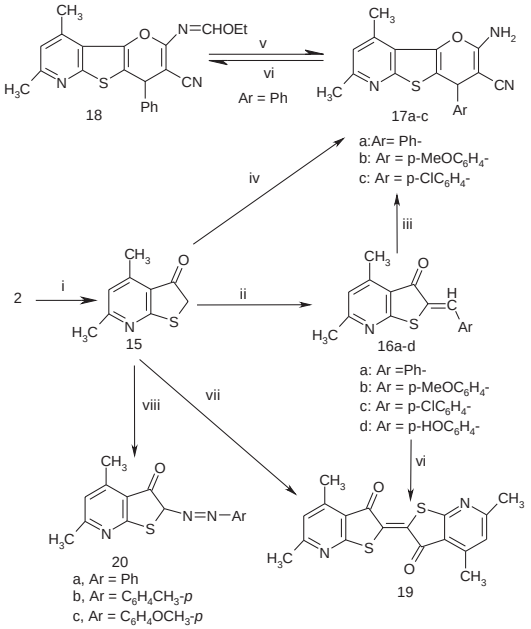
with amines or hydrazine hydrate, undergoes C=N bond fission to produce compound **17**. Attempts to synthesise 2-nitrosothieno-pyridin-3-one by reaction with nitrous acid leads to the formation of dimer **19** instead of the nitroso compound. The dimer **19** is also produced when we attempted to react the α,β-unsaturated compound **16** with hydrazines to synthesise 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** which then dimerises. The active methylene in compound **15** undergoes coupling with aryl diazonium chloride to give 2-arylazo-derivatives **20** (Scheme 3).



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 or NH_2NH_2; vii, $NaNO_2$/HCl; viii, ArN=NCl/EtOH/CH_2CO_2Na

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 in δ units. Mass spectra were recorded on a JEOL JMS 600 spectrometer. Elemental analyses were performed on a Perkin-Elmer 240C microanalyser. Compounds **1–3, 15** were prepared by the following procedure.[11]

General procedure for the synthesis of **4a–c:** A mixture of compound **3** (1.76 g, 0.01 mol) and arylldinemalononitrile (0.01 mol) in ethanol (30 ml), containing few drops of piperidine was heated under reflux for 3 h. The solid product which formed on heating was collected and recrystallised 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):** (78% yield), m.p. 298–300 °C. IR: ν_{max}/cm^{-1} 3400 (NH), 3200, 3100 (NH_2) 2220 (CN). ^{1}H NMR (DMSO-d_6): δ = 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):** (74% yield); m.p. 238–340 °C; IR: ν_{max}/cm^{-1} 3420, 3320 (NH_2), 3170 (NH) 2220 (CN). ^{1}H NMR (DMSO-d_6): δ 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):** (82% yield), m.p. 220–222 °C; IR: ν_{max}/cm^{-1} 3500 (NH), 3300, 3200 (NH_2) and 2210 (CN). ^{1}H NMR (DMSO-d_6): δ = 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]amino-acrylate **(5):** A mixture of compound **3** (1.76 g, 0.01 mol) and ethoxymethylene ethyl cyanoacetate (1.70 g, 0.01 mol) in ethanol (20 ml) containing a few drops of acetic acid was heated under reflux for 2 h, and then allowed to cool. The solid product was collected by filtration and recrystallised from ethanol as yellowish white crystals in 78% yield, m. p. 220–222 °C; IR: ν_{max}/cm^{-1} 3200 (NH), 2210 (CN) and 1700 cm^{-1} (C=O). ^{1}H NMR ($CDCl_3$): 1.4 (t, *J* = 9.3, 3H, CH_3), 2.6, 2.85 (2s, 6H, $2CH_3$), 4.35 (q, *J* = 6.3, 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** (1.5g, 0.005 mol) 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 recrystallised from dioxan as yellow crystals in 45% yield, m.p 310–312 °C; IR: ν_{max}/cm^{-1} 3150 cm^{-1} (NH), 2220 cm^{-1} (CN), 1700 cm^{-1} (C=O). ^{1}H NMR(DMSO-d_6): δ = 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 mol) and phenyl isothiocyanate (0.01 mol) in benzene (30 ml) was heated under reflux for 2 h., and then allowed to cool. The solid product was collected and recrystallised from ethanol as white crystals in 76% yield, m.p. 201–203 °C; IR: ν_{max}/cm^{-1} 3450, 3250 (2NH), 2950 (CH-aliphatic) 1500 (C=S). ^{1}H NMR (DMSO-d_6): δ= 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):** A solution of the thiourea derivative **7** (0.01 mol) in acetic acid (30 ml), was treated with bromine (0.01 mol) in acetic acid (10 ml) dropwise with stirring during 15 minutes. The stirring was continued for additional 1 hour and then water (100 ml) was added. The solid product was collected, washed well with water and recrystallised from ethanol as yellowish white crystals in 72% yield, m.p 199–200 °C. IR: ν_{max}/cm^{-1} 3300 (NH); ^{1}H NMR (DMSO-d_6): δ 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-4one **(9):** A mixture of compound **7** (3.13 g, 0.01 mol), ethyl chloroacetate (1.22 g, 0.01 mol) and sodium acetate (0.012 mol) in ethanol (30 ml) was heated under reflux for 4 h., then allowed to cool, poured into cold water (100 ml). The solid product was collected and recrystallised from ethanol as white crystals in 69% yield, m.p. 188–190 °C; IR: ν_{max}/cm^{-1} 1680 (C=O) and 1600 (C=N). ^{1}H NMR ($CDCl_3$): δ 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-methyl-acetate **(11):** A mixture of compound **10** (1.64 g, 0.01 mol), methyl 2-bromopropionate (1.67 g, 0.01 mol) and sodium acetate (0.012 mol) in methanol (30 ml) was refluxed for 2 h, then allowed to cool, poured into water. The solid product which formed was collected by filtration, recrystallised from a mixture of methanol/water (1:1) in 78% yield, m.p.64–66 °C ; IR: ν_{max}/cm^{-1} 2220 (CN), and 1710 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.5 (d, *J* = 9.0, 3H, CH_3), 2.3 (s, 6H, $2CH_3$), 3.3 (s 3H, CH_3). 4.35 (q, *J* = 6.3, 1H, CH). 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 mol). The reaction mixture then allowed to cool and poured into cold water (70 ml). The solid product was filtered off and recrystallised 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 mol), methyl-β-bromopropionate (1.67 g, 0.01 mol) and K_2CO_3 (0.02 mol in methanol (30 ml) was refluxed for 4 h. and then allowed to cool. The solid product was collected by filtration, and recrystallised from methanol as white crystals, in 70% yield, m.p. 126–128 °C; IR: ν_{max}/cm^{-1} 3350, 3250 (NH_2). ^1H NMR ($CDCl_3$): δ = 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 mol) and phenyl isothiocyanate (1.35 g, 0.01 mol) in benzene (30 ml) was refluxed for 5 h, then allowed to cool. The solid product was collected and recrystallised from ethanol as white crystals in 78% yield, m.p. 210–212 °C; IR: ν_{max}/cm^{-1} 3450 and 3250 (2NH). ^1H NMR($CDCl_3$): 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 mol), ethyl chloroacetate (1.22 g, 0.01 mol) and sodium acetate (0.012 mol) 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 recrystallised from ethanol as white crystals, in 67% yield, m.p. 227–230 °C; ^1H NMR ($CDCl_3$): δ = 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:** A mixture of compound **15** (0.01 mol) and the aryl aldehyde (0.01 mol) in ethanol (30 ml), containing a few drops of piperidine was heated under reflux for 2 h, then allowed to cool. The solid product was collected and recrystallised from dioxan.

2-Benzyledine-4,6-dimethyl-1,2-dihydrothieno[2,3-b]pyridin-3-one **(16a):** (77% yield), m.p. 174–176 °C; IR: ν_{max}/cm^{-1} 3050 (CH-aromatic) and 1690. ^1H NMR (DMSO-d_6): δ = 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-Dimethyl-1,2-dihydro-2-(4-methoxybenzyledine)thieno[2,3-b] pyridin-3-one **(16b)**: (85% yield), m.p. 182–184 °C; IR: ν_{max}/cm^{-1} 1690 (CO). ^1H NMR (DMSO-d_6): δ 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-dimethyl-1,2-dihydrothieno [2,3-b]pyridin-3-one **(16c): (**78% yield), m.p. 199–200 °C; Lit.[13] m.p. 198 °C.

4,6-Dimethyl-1,2-dihydro-2-(4-hydroxybenzyledine) thieno[2,3-b]pyridin-3-one **(16d):** (72% yield), m.p. > 300 °C; IR: ν_{max}/cm^{-1} 3450 (OH) 1690 (CO). ^1H NMR (DMSO-d_6): δ 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 mol) and malononitrile (0.01 mol) 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 recrystallised from ethanol.

Method b: A mixture of compound **15** (0.01 mol), arylidenemalononitrile (0.01 mol), and few drops of triethylamine as a catalyst in ethanol (30 ml) was refluxed for 3 h, then allowed to cool. The solid product was collected and recrystallised from ethanol.

2-Amino-7,9-dimethyl-4[H]-4-phenyl-pyrano[2',3':4,5] thieno[2,3-b]pyridine-3-carbonitrile **(17a):** (78% yield), m.p. 265–268 °C; IR: ν_{max}/cm^{-1} 3340, 3230 (NH_2), 2210 (CN). ^1H NMR ($CDCl_3$): 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): (87% yield), m.p. 183–185 °C; IR: ν_{max}/cm^{-1} 3360, 3260 (NH_2), 2220 (CN). ^1H NMR (DMSO-d_6): δ = 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: ν_{max}/cm^{-1} 3380, 3280 (NH_2), 2220 (CN). ^1H NMR (DMSO-d_6): δ = 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 mol) and triethyl orthoformate (0.02 mol) in acetic anhydride (20 ml) was heated under reflux for two hours, then allowed to cool and poured into (100 ml). The solid product was collected and recrystallised from ethanol as white crystals (72 % yield), m.p 210–213°C; IR: ν_{max}/cm^{-1} 2220 (CN). ^1H NMR ($CDCl_3$): δ 1.4–1.6 (t, *J* = 9.0, 3H, CH_3), 2.5. 2.7 (2s, 6H, CH_3). 4.3–4.6 (q. *J* = 6.3, 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 mol) and phenylhydrazine (1.08 g, 0.01 mol) in ethanol (30 ml) was heated under reflux for 3 h. The red crystals which precipitated while heating, were filtered off hot and identified as compound **19**. The filtrate was evaporated and the residue was identified as benzylidine phenylhydrazone.

Method b: To a stirred solution of compound **15** (1.79 g, 0.01 mol) in acetic acid (20 ml), sodium nitrite solution (0.02 mol) in water (5 ml) was added dropwise during 10 minute. The solid product was collected and recrystallised from dioxan in 78% yield and identified as compound **19**. Red crystals in 65% yield, m.p. > 300 °C; IR: ν_{max}/cm^{-1} 1680 (C=O). ^1H NMR(CF_3CO_2D): 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-dimethylthieno[2,3-b]pyridin-3-one **(20):** To a solution of compound **15** (1.79 g, 0.01 mol) in ethanol containing 0.05 mol sodium acetate, a solution of diazotised aromatic amine (0.01 mol) was added dropwise with stirring at 5 °C for 16 minutes. After addition was finished the stirring was continued for one hour, then allowed to stand for 2 h. The solid product was collected and recrystallised from ethanol.

4,6-Dimethyl-2-phenylazothieno[2,3-b]pyridin-3-one **(20a):** (78% yield), m.p. 178 °C; IR: ν_{max}/cm^{-1} 3350 (NH). 1680 (C=O). ^1H NMR($CDCl_3$); δ = 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-Dimethyl-2-(4-methylphenyl)-azothieno[2,3-b]pyridin-3-one **(20b):** (76% yield), m.p. 180 °C; IR: ν_{max}/cm^{-1} 3350 (NH). 1680 (C=O). ^1H NMR($CDCl_3$); δ = 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-Dimethyl-2-(4methoxyphenyl)-azothieno[2,3-b]pyridin-3-one **(20c):** (82% yield), m.p. 205 °C; IR: ν_{max}/cm^{-1} 3350 (NH). 1680 (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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