Convenient synthesis and reactions of some 7,9-dimethylthieno-[2,3-*b*:4,5-*b′*]dipyridines

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3-Amino-4,6-dimethylthieno[2,3-*b*]pyridine-2-carboxaldehyde was prepared and from it various functionalised thieno[2,3-*b*:4,5-*b*']dipyridines were synthesised, using the Friedländer and related reactions. Ethyl 2,7,9-trimethylthieno[2,3-*b*:4,5-*b*']dipyridine-3-carboxylate was transformed into a variety of thieno[2,3-*b*:4,5-*b*']dipyridine systems with heterocyclic rings attached at C-3 or fused at C2–C3.

Keywords: pyrazoles, 1,3,4-oxadiazoles, fused pyridines, thiophenes, pyrroles, quinolines, pyridazines, Friedländer reactions

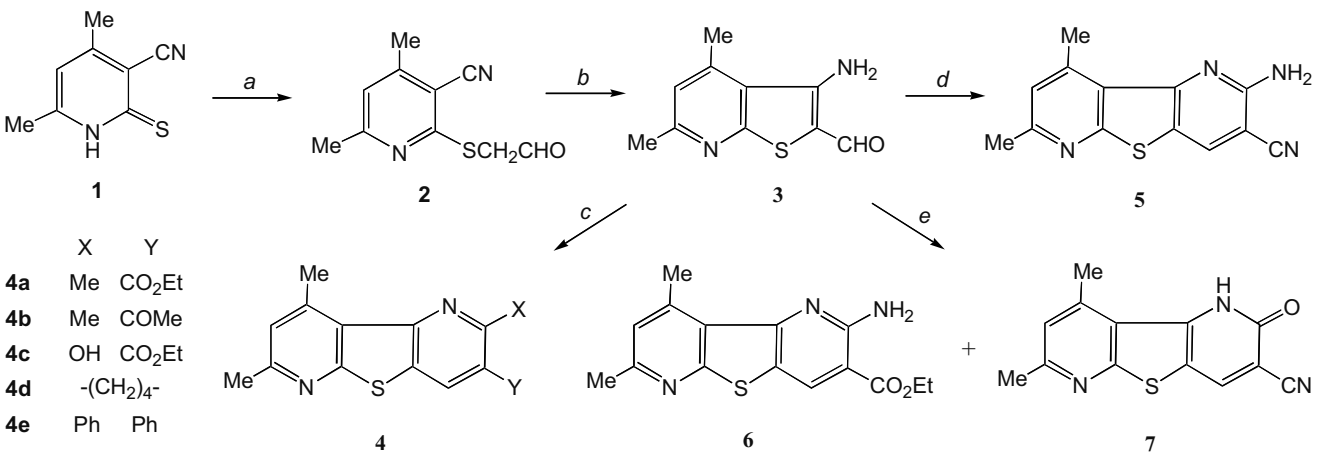
Fused pyridines and, in particular, thienopyridines are well-known as biologically active compounds. Thus, in the series of thienopyridines and related condensed analogues, antithrombotic,[1,2] antihistamine (antianaphylactic),[3] antibacterial,[4] antiallergic[5] and neuroprotective[6] agents have been found. Polysubstituted and partially hydrogenated pyridothienopyridines are new heterocycles with potential biological activity.[7,8] Their syntheses, however, are based on a multistep approach and often require inaccessible reagents. In continuation of our work in the synthesis and studies of thienopyridines[9-11] and pyridothienopyridines (thienodipyridines),[12] we report here a new approach to the synthesis of thieno[2,3-*b*:4,5-*b′*]dipyridines.

Results and discussion

Reaction of 4,6-dimethyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (**1**) with chloroacetaldehyde in ethanolic sodium hydroxide afforded 2-(3-cyano-4,6-dimethylpyridin-2-ylthio)acetaldehyde (**2**), which cyclised in the presence of sodium ethoxide to give 3-amino-4,6-dimethylthieno [2,3-*b*]pyridine-2-carbaldehyde (**3**). The IR spectrum of compound **2** showed a C≡N absorption band at 2210 cm^{-1}, which disappeared when cyclised to give the thienopyridine **3** and was replaced by bands at 3430 and 3310 cm^{-1} for NH_2. The ^1H NMR of **2** showed a CHO group and a signal at δ 3.7 for CH_2 which disappeared when compound **2** cyclised to form the thienopyridine **3**, then showing a new signal at 6.8 for NH_2.

Compound **3** underwent Friedländer reactions with various reagents, specifically ethyl acetoacetate, acetyl acetone and diethyl malonate, in ethanol in the presence of catalytic piperidine to give thieno[2,3-*b*:4,5-*b*']dipyridine derivatives **4a–c** in good yields. Also it reacted with cyclohexanone and deoxybenzoin in ethanol in the presence of sodium hydroxide to give 2,4-dimethyl-6,7,8,9-tetrahydropyrido[2',3':2,3]thieno-[4,5-*b*]quinoline (**4d**) in 78% yield and 7,9-dimethyl-2,3-diphenylthieno[2,3-*b*:4,5-*b*']dipyridine (**4e**) in 64% yield, respectively. The IR spectra of **4a–e** revealed the disappearance of bands characteristic of NH_2 in the starting material and the appearance of absorption at 1715 cm^{-1} of the ester carbonyl group in **4a** and at 1700 cm^{-1} for the ketonic carbonyl group in **4b**; and in the case of **4d** and **4e** showed the disappearance of bands characteristic of NH_2 and aldehydic carbonyl groups in the starting material. The ^1H NMR of **4a** showed triplet and quartet signals at 1.40 and 4.33 characteristic of the OEt group, methyl singlets at δ 2.6 (3H) and 2.9 (6H), and two singlets at δ 6.95 and 8.45 for the pyridine protons. The mass spectrum of **4a** showed the molecular ion as base peak at *m/z* 300. The ^1H NMR of **4b** revealed new signals at δ 2.6 and 3.0 for Me and COMe protons.

The amino-carboxaldehyde **3** was allowed to react with malononitrile in ethanol in the presence of piperidine as catalyst; 2-amino-7,9-dimethylthieno[2,3-*b*:4,5-*b*']dipyridine-3-carbonitrile (**5**) was produced. The IR of compound **5** showed absorption bands at 3450 and 3350 cm^{-1} for NH_2 and at 2200 for CN.



Scheme 1 *Reagents and conditions: a,*: $ClCH_2CHO$/EtOH/NaOH, 10 °C; *b*, EtONa/EtOH, reflux; *c,*: $XCOCH_2Y$; *d,*: $CH_2(CN)_2$; *e*, $NCCH_2CO_2Et$; *c-e:* all in piperidine/EtOH, reflux.

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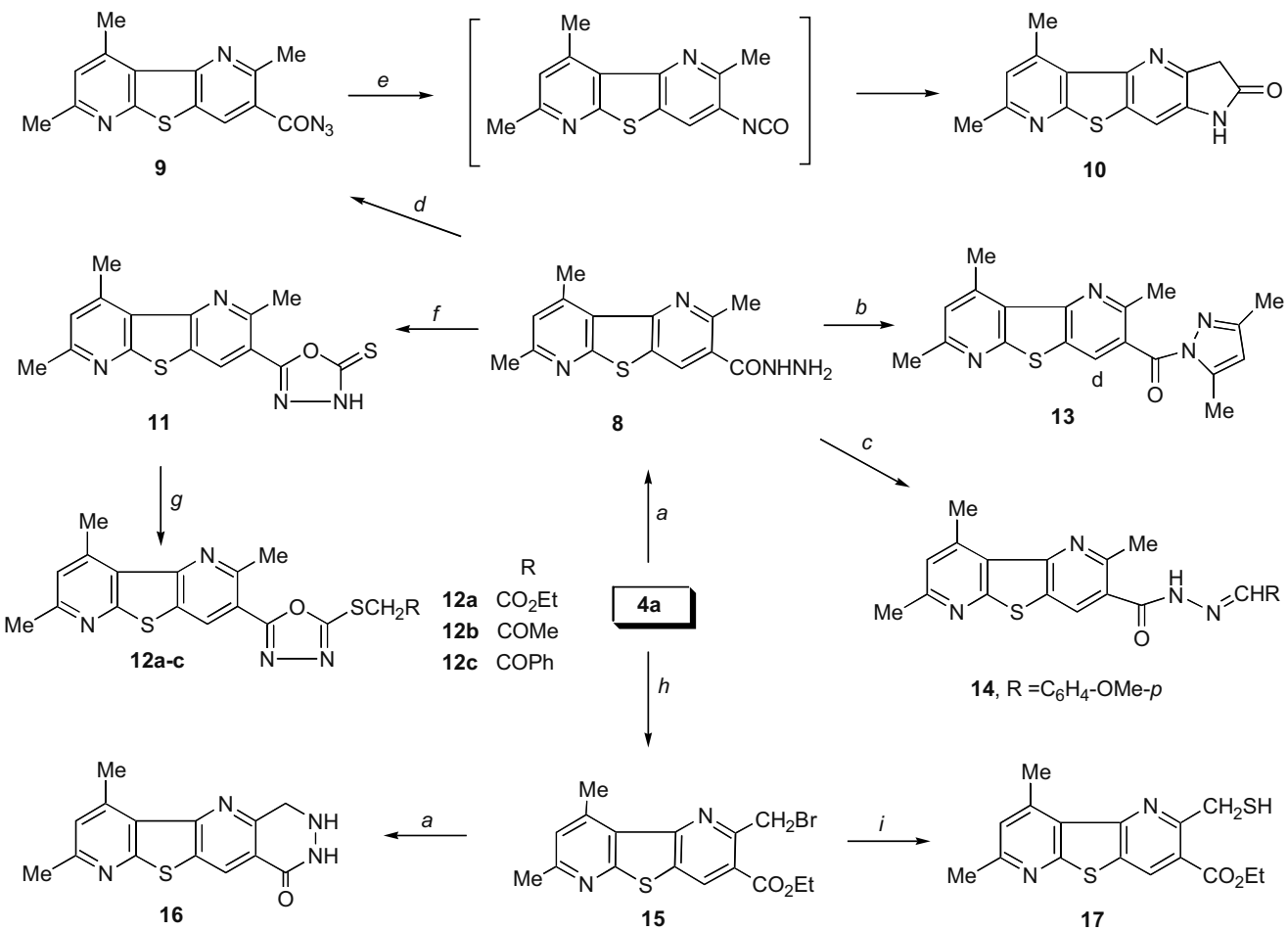
When ethyl cyanoacetate was used instead of malononitrile, a mixture of ethyl 2-amino-7,9-dimethylthieno[2,3-*b*:4,5-*b*']dipyridine-3-carboxylate (**6**) and 7,9-dimethyl-2-oxo-1,2-dihydrothieno[2,3-*b*:4,5-*b*']dipyridine-3-carbonitrile (**7**) was formed (Scheme 1).The mixture of **6** and **7** was separated by column chromatography using ethyl acetate: methylene chloride (1 : 1) as eluent in 48 and 38% yields. The IR of compound **6** showed bands at 3420 and 3320 cm^{-1} for NH_2 and 1690 for C=O. The ^1H NMR revealed a triplet at δ 1.5 for CH_3 and a quartet at 4.55 for the ethyl ester. The MS showed a peak at *m/z* 300 (M^+–1, 100%).

Hydrazinolysis of compound **4a** using hydrazine hydrate in ethanol afforded the trimethylthieno[2,3-*b*:4,5-*b*']dipyridine-8-carbohydrazide **8**. Its IR showed bands at 3350–3200 ($NHNH_2$) and 1650 cm^{-1} (C=O) The ^1H NMR showed the disappearance of signals characteristic of the ethoxy group present in the starting material and the appearance of signals at δ 4.5 for NH_2 and 8.9 for NH which were exchangeable with D_2O. (Scheme 2)

Carbohydrazide **8** was converted into 2,7,9-trimethylthieno[2,3-*b*:4,5-*b*']dipyridine-3-carboazide (**9**) by treatment with nitrous acid in acetic acid at 0-5 °C. The IR showed bands at 2150 (N_3) and 1700 cm^{-1} (C=O). When the azide **9** was heated in xylene it first underwent a Curtius rearrangement to give an intermediate isocyanate, followed by cyclisation to the adjacent methyl group to produce the pyrrolopyridothienopyridine **10**. The ^1H NMR of compound **10** showed the presence of a 2H singlet signal at δ 3.3 for the methylene group and at 5.4 a signal for NH exchangeable by D_2O.

Heating the carbohydrazide **8** with carbon disulfide in pyridine on a steam bath afforded 5-(2,7,9-trimethylthieno[2,3-*b*:4,5-*b*']dipyridin-3-yl)-1,3,4-oxadiazole-2(3*H*)-thione (**11**) in fair yield. The thione **11** was alkylated using α-halogenated carbonyl compounds, *viz.* ethyl chloroacetate, phenacyl bromide and chloroacetone, to afford compound **12a–c** respectively. IR of compounds **12a–c** revealed no band characteristic of the NH group in the starting material and showed the appearance of new carbonyl absorption bands. Also, compound **8** condensed with acetylacetone and with anisaldehyde to give the *N*-acylpyrazole **13** and the acylhydrazone **14**, respectively (Scheme 2).

Treatment of the ester **4a** with bromine in acetic acid in the presence of sodium acetate resulted in bromination of the methyl group adjacent to the ester function to give ethyl 2-bromomethyl-7,9-dimethylthieno[2,3-*b*:4,5-*b*']dipyridine-3-carboxylate (**15**). The NMR of showed a signal at δ 4.0 for the CH_2Br group. Compound **15**, when refluxed with hydrazine hydrate, underwent nucleophilic substitution of bromine by hydrazine followed by cyclisation with elimination of ethanol to give 2,4-dimethyl-6,7,8,9-tetrahydropyrido[2",3":2',3']thieno-[4',5':2,3]pyrido[5,6-*d*]pyridazine (**16**) in 60% yield. The IR of compound **16** showed the ester carbonyl group replaced by a band at 1660 cm^{-1}; the ethoxy signals in the NMR were also absent. Furthermore, the bromine atom in compound **15** was exchanged by a SH group on reflux with thiourea followed by treatment with sodium hydroxide solution and then acidification with dilute HCl. (Scheme 2)



Scheme 2 *Reagents and conditions*: *a,* $N_2H_4.H_2O$/EtOH, reflux; *b,* $(Ac)_2CH_2$/EtOH; *c,* anisaldehyde/EtOH/AcOH, Δ; *d*, $NaNO_2$, AcOH at 5-10 °C; *e,* xylene, Δ; *f,* CS_2/pyridine, steam bath; *g,* $RCH_2Cl(Br)$/EtOH/AcONa; *h,* Br_2/AcOH/AcONa; *i,* thiourea/EtOH, Δ, then $NaOH/H_2O$, then dil. HCl.

Experimental

Melting points were measured on a Fisher–Johns apparatus. Elemental analyses (C, H, N and S) were determined on an Elementar Analysensystem GmbH-VarioEL V.3 microanalyser in the central laboratory of Assiut University. The IR spectra were obtained on a Pye-Unicam SP-100 spectrophotometer using the KBr disc technique. NMR spectra were recorded on a Varian EM-390 90 MHz spectrometer in a suitable deuteriated solvent using TMS as internal standard (chemical shifts in ppm). MS spectra were recorded on JEOL JMS-600 apparatus.

2-(3-Cyano-4,6-dimethylpyridin-2-ylthio)acetaldehyde (**2**): To a solution of 4,6-dimethyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (**1**)[13] (1.64 g, 0.01 mol) in sodium hydroxide (20 mL, 10%) chloroacetaldehyde (50% solution, 2 mL) was added and the reaction mixture was stirred at room temperature for 10 h. After dilution with water (100 mL) the solid product was collected and recrystallised from ethanol as yellowish crystals (1.2 g, 58%), m.p. 100 °C. IR: ν_{max} 2210 (CN), 1720 cm^{-1} (C=O). NMR ($CDCl_3$): δ_H 2.5, 2.6 (2 s, 6H, $2CH_3$), 3.9 (2H, CH_2), 6.9 (s, 1H, CH pyridine), 9.5 (1H, CHO). Anal. Calcd for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.89; N, 13.58; S, 15.54. Found: C, 58.01; H, 5.09; N, 13.71; S, 15.32%.

3-Amino-4,6-dimethylthieno[2,3-b]pyridine-2-carbaldehyde (**3**): The acetaldehyde derivative **2** (2.1 g, 0.01 mol) was stirred at room temperature for 5 h in ethanol (20 mL) containing sodium ethoxide (1.36 g, 0.02 mol). Dilution with water (100 mL) precipitated a solid product which was collected and recrystallised from ethanol as brown crystals (2 g, 95%), m.p. 130 °C. IR: ν_{max} 3520, 3410 (NH_2), 1670 cm^{-1} (C=O). ^{1}H NMR (DMSO-d_6): 2.5, 2.7 (2 s, $2CH_3$), 6.8 (s, NH_2), 7.15 (s, pyridine CH) and 9.7 (s, 1H, CHO). Anal. Calcd for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.89; N, 13.58; S, 15.54. Found: C, 58.42; H, 4.69; N, 13.72; S, 15.71%.

7,9-Dimethylthieno[2,3-b:4,5-b']dipyridines (**4a–c**); *general procedure*
The amino-aldehyde **3** (1.0 g, 5 mmol) was heated for 4 h under reflux in ethanol (20 mL) containing a few drops of piperidine with the appropriate α-methylene carbonyl compound (ethyl acetoacetate, pentane-2,4-dione, or diethyl malonate, 5 mmol). After cooling, the solid product was filtered off and recrystallised from the indicated solvent.

Ethyl 2,7,9-trimethylthieno[2,3-b:4,5-b']dipyridine-3-carboxylate (**4a**): White crystals (1.2 g, 87%) from ethanol, m.p. 160–162 °C. IR: ν_{max} 2950 (CH aliphatic) and 1710 cm^{-1} (C=O). NMR ($CDCl_3$): δ_H 1.40 (t, CH_3 of OEt), 2,6 (s, CH_3), 2.9 (2 s, $2CH_3$), 4.33 (q, CH_2 of OEt), 6.95, 8.45 (2 s, 2CH pyridine). MS: *m/z* (%) 300 (M^+, 100), 272 $(M - C_2H_4)^+$, 255 $(M - OEt)^+$, 227 $(M - CO_2Et)^+$. Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33; S, 10.67. Found: C, 64.19; H, 5.60; N, 9.54; S, 10.45%.

3-Acetyl-2,7,9-trimethylthieno[2,3-b:4,5-b']dipyridine (**4b**): White crystals (1.05 g, 78%) from ethanol, m.p. 163–165 °C. NMR ($CDCl_3$): δ_H 2.6 (s, $2CH_3$), 2.85 (s, CH_3), 3.0 (s, CH_3), 7.0, 8.35 (2 s, 2 CH pyridine). Anal. Calcd for $C_{15}H_{14}N_2OS$: C, 66.64; H, 5.22; N, 10.36; S, 11.86. Found: C, 66.86; H, 5.00; N, 10.526; S, 12.08%.

2-Hydroxy-7,9-dimethylthieno[2,3-b:4,5-b']dipyridine-3-carboxylate (**4c**): Yellowish white solid (1.0 g, 66%), from dioxan, m.p > 300 °C. IR: ν_{max} 2400 (OH) and 1690–1660 cm^{-1} (C=O). NMR ($CDCl_3$): δ_H 1.35 (t, CH_3 ester), 2,5 (s, CH_3), 2.9 (2 s, $2CH_3$), 4.4 (q, CH_2 ester), 6.95, 8.55 (2 s, 2CH pyridine), 10 (s, OH). Anal. Calcd for $C_{15}H_{14}N_2O_3S$: C, 59.59; H, 4.67; N, 9.27; S, 10.60. Found: C, 59.78; H, 4.89; N, 9.03; S, 10.38%.

2,4-Dimethyl-6,7,8,9-tetrahydropyrido[2',3':2,3]thieno[4,5-b]quinoline (**4d**): Compound **3** (1 g, 5 mmol) and cyclohexanone (0.5 g, 5 mmol) were stirred together in ethanolic sodium hydroxide (10%, 20 mL) room temperature for 6 h, and then water (100 mL) was added. The solid product that separated was collected and recrystallised from ethanol, forming white crystals (1.0 g, 78%), m.p 158–160 °C. NMR (MHz, $CDCl_3$): δ_H 1.8 (m, $2CH_2$), 2.5, 2.7 (2 s, $2CH_3$), 2.95 (m, $2CH_2$), 6.95, 7.8 (2 s, pyridine H). MS: *m/z* (%) 268 (M^+, 100). Anal. Calcd for $C_{16}H_{16}N_2S$: C, 71.61; H, 6.01; N, 10.44; S, 11.95. Found: C, 71.38; H, 5.79; N, 10.66; S, 12.17%.

7,9-Dimethyl-2,3-diphenylthieno[2,3-b:4,5-b']dipyridine (**4e**): The synthetic procedure was similar to described above, employing deoxybenzoin (5 mmol) instead of cyclohexane. Compound **4e** (1.17 g, 64%) m.p. 290 °C. NMR (CF_3CO_2D): δ_H 2.7, 3.0 (2 s, $2CH_3$), 7.1–7.5 (m, 5H, ArH), 7.0, 8.1 (2 s, pyridine H). Anal. Calcd for $C_{24}H_{18}N_2S$: C, 78.66; H, 4.95; N, 7.64; S, 8.75. Found: C, 78.90; H, 5.16; N, 7.41; S, 8.52%.

2-Amino-7,9-dimethylthieno[2,3-b:4,5-b']dipyridine-3-carbonitrile (**5**): To compound **3** (1.0 g, 5 mmol) and malononitrile (0.33 g, 005 mol) in ethanol (25 mL), a few drops of piperidine were added. The mixture was heated under reflux for 3 h, and then allowed to cool. The solid product was collected and recrystallised from dioxan as brown crystals (0.85 g, 67%), m.p. 200–202 °C. IR: ν_{max} 3450, 3350 (NH_2), 2200 cm^{-1} (CN). NMR (DMSO-d_6): δ_H 2,5 (s, CH_3), 2.9 (2 s, $2CH_3$), 6.8 (s, NH_2), 7.0, 8.50 (2 s, 2 CH-pyridine). MS: *m/z* (%) 254 (M^+, 100%). Anal. Calcd for $C_{13}H_{10}N_4S$: C, 61.40; H, 3.96; N, 22.03; S, 12.61. Found: C, 61.63; H, 4.18; N, 21.80; S, 12.84%.

Ethyl 2-amino-7,9-dimethylthieno[2,3-b:4,5-b']dipyridine-3-carboxylate (**6**) *and 7,9-Dimethyl-2-oxo-1,2-dihydrothieno[2,3-b:4,5-b']dipyridine-3-carbonitrile* (**7**): To compound **3** (1.0 g, 5 mmol) and ethyl cyanoacetate (0.57 g, 005 mol) in ethanol (15 mL), a few drops of piperidine was added. The mixture was heated under reflux for 3 h, and then allowed to cool. The solid product was collected and chromatographed on silica gel using ethyl acetate as eluent to give the ester **6** as yellowish orange crystals (0.72 g, 48%), m.p. 198–200 °C, and the nitrile **7** as red crystals m.p 238 °C. (0.49 g, 38%).

Compound **6**: IR: ν_{max} 3420, 3320 (NH_2), 1690 cm^{-1} (CO). ^{1}H NMR (DMSO-d_6): δ_H 1.5 (t, CH_3), 2.55, 2.9 (2 s, $2CH_3$), 4.55 (q, CH_2), 6.5 (s, NH_2), 7.0, 8.5 (2 s, CH pyridine). MS: *m/z* (%) 300 (M^+–1, 100%). Anal. Calcd for $C_{15}H_{15}N_3O_2S$: C, 59.78; H, 5.02; N, 13.94; S, 10.64. Found: C, 60.01; H, 4.83; N, 14.17; S, 10.81%.

Compound **7**: IR: ν_{max} 3350 (NH), 2220 (CN), 1670 cm^{-1} (CO). NMR (CF_3CO_2D): δ_H 2.7, 3.2 (2 s, $2CH_3$), 7.2, 8.5 (2 s, CH pyridine). MS: *m/z* (%) 254 (M^+–1, 100%). Anal. Calcd for $C_{13}H_9N_3OS$: C, 61.16; H, 3.55; N, 16.46; S, 12.56. Found: C, 60.93; H, 3.32; N, 16.67; S, 12.76%.

2,7,9-Trimethylthieno[2,3-b:4,5-b']dipyridine-3-carbohydrazide (**8**): The ester **4a** (3 g, 0.01 mol) and hydrazine hydrate (80%, 1.9 mL, 0.03 mol) in ethanol (20 mL) were heated under reflux for 5 h, and then allowed to cool. The solid product was collected as yellowish crystals (2.1 g 74%), m.p. 260 °C. IR: ν_{max} 3350–3200 ($NHNH_2$) and 1650 cm^{-1} (C=O). NMR (DMSO-d_6): δ_H 2.3, 2.5, 2.9 (3 s, 3 CH_3), 4.5 (broad, NH_2), 6.9, 8.0 (s, 2CH pyridine), 8.9 (s, NH). Anal. Calcd for $C_{14}H_{14}N_4OS$: C, 58.72; H, 4.93; N, 19.57; S, 11.20. Found: C, 58.95; H, 5.16; N, 19.39; S, 11.00%.

2,7,9-Trimethylthieno[2,3-b:4,5-b']dipyridine-8-carboazide (**9**): The hydrazide **8** (1.43 g, 5 mmol) was dissolved in acetic acid (10 mL), cooled to 5–10 °C, and sodium nitrite (0.69 g, 0.01 mol) in H_2O (2 mL) was added dropwise with stirring over 10 minutes. The reaction mixture was allowed to stand for 2 h, and the solid product (1.17 g, 79%), m.p. 140 °C (decomp.), was filtered off and used without further purification. IR: ν_{max} 2150 (N_3) and 1700 cm^{-1} (C=O). ^{1}H NMR ($CDCl_3$): δ_H 2.6 (s, CH_3), 2.9 (2 s, $2CH_3$), 6.95, 9.2 (2 s, 2CH pyridine).

7,9-Dimethyl-1,3-dihydro-2H-pyrrolo[3,2-b]thieno[2,3-b:4,5-b']dipyridin-2-one (**10**): The carboazide **9** (1.0 g, 4 mmol) (15 mL) was heated under reflux in dry xylene for 1 h. The solid product which separated while hot was filtered off and recrystallised from dioxan as brown crystals (0.88 g, 82%), m.p >300 °C. IR: ν_{max} 3250 (NH) and 1600 cm^{-1} (C=O). NMR (DMSO-d_6): δ_H 2.55, 2.9 (2 s, $2CH_3$), 5.4 (s, NH), 6.95 and 8.5 (2 s, 2CH pyridine). Anal. Calcd for $C_{14}H_{11}N_3OS$: C, 62.44; H, 4.12; N, 15.60; S, 11.91. Found: C, 62.28; H, 4.34; N, 15.83; S, 12.14%.

5-(2,7,9-Trimethylthieno[2,3-b:4,5-b']dipyridin-3-yl)-1,3,4-oxadiazole-2(3H)-thione (**11**): The carbohydrazide **8** (1.43 g, 5 mmol) and carbon disulfide (1 mL) in pyridine (10 mL) were heated on a steam bath for 8 h, then allowed to cool. The solid product which separated was collected and recrystallised from ethanol as yellowish crystals (1.2 g, 74%), m.p. >300 °C. IR: ν_{max} 3400 cm^{-1} (NH). NMR (CF_3CO_2D): δ_H 2.65, 2.75, 3.0 (3 s, $3CH_3$), 7.1, 8.3 (2 s, CH pyridine). Anal. Calcd for $C_{15}H_{12}N_4OS_2$: C, 54.86; H, 3.68; N, 17.06; S, 19.53. Found: C, 55.09; H, 3.81; N, 16.86; S, 19.75%.

Alkylation of the thione **11**: *general procedure*
The compound **11** (1.6 g, 5 mmol), the halogenated compound (5 mmol) and sodium acetate (0.5 g, 0.06 mmol) were heated to reflux in ethanol for 2 h, then allowed to cool. The solid product **12** was filtered off, washed with water several times, dried and recrystallised from ethanol.

Ethyl 2-[5-[(2,7,9-trimethylthieno[2,3-b:4,5-b']dipyridin-3-yl)-[1,3,4]oxadiazol-2-yl]sulfanyl]acetate (**12a**): White crystals (1.76 g, 85%), m.p 188–190 °C. IR: ν_{max} 2950 (CH aliphatic), 1725 cm^{-1} (CO). NMR ($CDCl_3$): δ_H 1.3 (t, CH_3 ester), 2.6 (s, CH_3), 3.0 (s, $2CH_3$), 4.15 (q, CH_2 ester), 7.0, 8.5 (2 s, 2CH pyridine). Anal. Calcd for $C_{19}H_{18}N_4O_3S_2$: C, 55.06; H, 4.38; N, 13.52; S, 15.47. Found: C, 54.88; H, 4.61; N, 13.75; S, 15.33%.

1-[[5-(2,7,9-Trimethylthieno[2,3-b:4,5-b']dipyridin-3-yl)-1,3,4-oxadiazol-2-yl]sulfanyl]propan-2-one (**12b**): White crystals (1.65 g, 86%), m.p. 230–232 °C. IR: ν_{max} 2950 (CH aliphatic), 1700 cm^{-1} (CO). NMR (CF_3CO_2D): δ_H 2.7, 3.1, 3.3, 3.55 (4 s, $4CH_3$), 4.6 (s,

SCH_2), 7.9, 9.1 (2 s, CH pyridine). Anal. Calcd for $C_{18}H_{16}N_4O_2S_2$: C, 56.23; H, 4.19; N, 14.57; S, 16.68. Found: C, 56.00; H, 4.36; N, 14.72; S, 16.46%.

2-[[5-(2,7,9-Trimethylthieno[2,3-b:4,5-b']dipyridin-3-yl)-1,3,4-oxadiazol-2-yl]sulfanyl]-1-phenylethanone (**12c**): White crystals (1.8 g, 80%), m.p. 200–202 °C. IR: ν_{max} 3050 (CH aromatic), 1690 cm^{-1} (CO). NMR (CF_3CO_2D): δ_H 2.7, 2.9, 3.0 (3 s, $3CH_3$), 4.3 (s, SCH_2), 7.1, 8.7 (2 s, CH-pyridine), 7.4–8.2 (m, Ar-H). Anal. Calcd for $C_{23}H_{18}N_4O_2S_2$: C, 61.86; H, 4.06; N, 12.55; S, 14.36. Found: C, 62.05; H, 4.27; N, 12.33; S, 14.14%.

1-(2,7,9-Trimethylthieno[2,3-b:4,5-b']dipyridine-3-carbonyl)-3,5-dimethylpyrazole (**13**): The hydrazide **8** (1.43 g, 5 mmol) and acetyl acetone (0.05 g, 5 mmol) were refluxed for 5 h in ethanol (15 mL), then allowed to cool. The solid product was filtered off and recrystallised from ethanol as yellowish white crystals (1.35 g, 77%) yield, m.p 180 °C. IR: ν_{max} 1680 cm^{-1} (CO). NMR ($CDCl_3$): δ = 2.3, 3.05, 3.15 (3 s, $3CH_3$), 2.9 (s, $2CH_3$), 6.2 (s, CH-pyrazole), 7.1, 8.2 (2 s, 2CH pyridine). Anal. Calcd for $C_{19}H_{18}N_4OS$: C, 65.12; H, 5.18; N, 15.99; S, 9.15. Found: C, 64.88; H, 5.39; N, 16.22; S, 8.94%.

*N′-Anisylidene 2,7,9-trimethylthieno[2,3-b:4,5-b']dipyridine-3-carbohydrazide (***14**): The hydrazide **8** (1.43 g, 5 mmol) and anisaldehyde (0.68 g, 5 mmol) in ethanol (15 mL) were mixed, and a few drops of acetic acid were added. The mixture was heated to reflux for 3 h, and then allowed to cool. The solid product was filtered off and recrystallised from ethanol as yellow–white crystals (1.7 g, 86%), m.p. 268–270 °C. IR: ν_{max} 3350 (NH), 1670 cm^{-1} (CO). NMR (DMSO-d_6): δ_H 2.3, 2.5, 2.9 (3 s, $3CH_3$), 3.9 (s, OCH_3), 6.8, 7.2 (2 d, CHaromatic), 7.0, 8.5 (2 s, 2CH pyridine), 11.5 (s, NH). Anal. Calcd for: $C_{22}H_{20}N_4O_2S$: C, 65.33; H, 4.98; N, 13.85; S, 7.93. Found: C, 65.11; H, 5.21; N, 13.63; S, 8.14%.

Ethyl 2-bromomethyl-7,9-dimethylthieno[2,3-b:4,5-b']dipyridine-3-carboxylate (**15**): To the ester **4a** (1.5 g, 5 mmol) and sodium acetate (1 g, 0.012 mol) in acetic acid (20 mL), bromine (1 g. 0.006 mol) in acetic acid (5 mL) was added dropwise with stirring over 15 min. After addition was complete stirring was continued for an additional 1 h. The reaction mixture was poured into cold water (100 mL). The solid product was filtered off and recrystallised from ethanol as yellow crystals (1.5 g, 80%), m.p 154–156 °C. IR: ν_{max} 1720 cm^{-1} (CO). NMR ($CDCl_3$): δ_H 1.3(t, CH_3 ester), 4.5 (q, CH_2 ester), 2.5, 2.8 (2 s, $2CH_3$), 4.0 (s, CH_2Br), 7.0, 8.6 (2 s, 2CH pyridine). Anal. Calcd for $C_{16}H_{15}BrN_2O_2S$: C, 50.67; H, 3.99; Br, 21.07; N, 7.39; S, 8.45. Found: C, 50.88; H, 4.23; Br, 20.86; N, 7.61; S, 8.65%.

2,4-Dimethyl-7,8-dihydropyrido[2",3":2',3']thieno[4',5':2,3]-pyrido[5,6-d]pyridazin-9(6H)-one (**16**): The bromomethyl compound **15** (1.9 g, 5 mmol) in hydrazine hydrate (80%, 5 mL) was heated under reflux for 2 h, then ethanol (20 mL) was added and reflux was continued for additional 2 h, then allowed to cool. Afte collection and and recrystallisation from ethanol the solid product (0.85 g, 60%) had m.p 240–242 °C. IR: ν_{max} 3450, 3240 (2NH), 1660 cm^{-1} (CO). NMR (DMSO-d_6): δ_H 2.5, 2.9 (2 s, $2CH_3$), 3.2 (s, CH_2), 7.1, 8.3 (2 s, 2CH pyridine), 9.6, 10.5 (2 s, 2NH). Anal. Calcd for $C_{14}H_{12}N_4OS$: C, 59.14; H, 4.25; N, 19.70; S, 11.28. Found: C, 58.91; H, 4.02; N, 19.94; S, 11.05%.

Ethyl 2-mercaptomethyl-7,9-dimethylthieno[2,3-b:4,5-b']dipyridine-3-carboxylate (**17**): The bromomethyl compound **15** (1.9 g, 5 mmol) in ethanol (20 mL) was heated under reflux for 5 h with an excess of thiourea (0.76 g, 0.01 mol), and then allowed to cool. The solid product was filtered off and washed several times with water to remove unreacted thiourea. The residue was dissolved in aqueous NaOH (20 mL, 10%) and then acidified with HCl (0.1 N) to just neutral. The solid precipitated product was collected and recrystallised from ethanol as yellow crystals (1.16 g, 70%), m.p 170–172 °C. IR: ν_{max} 2550 (SH), 1710 cm^{-1} (CO). NMR (DMSO-d_6): δ_H 1.4 (t, CH_3 ester), 2.5, 2.85 (2 s, $2CH_3$), 4.3 (s, CH_2), 4.45 (q, CH_2 ester), 7.1, 8.7 (2 s, 2CH pyridine). Anal. Calcd for $C_{16}H_{16}N_2O_2S_2$: C, 57.81; H, 4.85; N, 8.43; S, 19.29. Found: C, 57.80; H, 4.65; N, 8.42; S, 19.51%.

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