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Synthesis and structure of some thienopyrimidine derivatives

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Abstract A series of substituted thieno[2,3-*d*]pyrimidines was synthesized starting from ethyl-2-amino-4-isopropylthiophene-3-carboxlate. Reaction of 2-hydrazino-5-isopropyl-thieno[2,3-*d*]pyrimidin-4(3H)-one and its 3-methyl analogue with different reagents afforded thieno[2,3-*d*]triazolo[4,3-*a*]pyrimidines and thieno[3,2-*e*]triazolo[4,3-*a*]pyrimidines, beside open chain derivatives.

Keywords Thieno[2,3-*d*]pyrimidines; Thieno[2,3-*d*]triazolo-[4,3-*a*]pyrimidines; Thieno[3,2-*e*]triazolo[4,3-*a*]pyrimidines; Thieno[3,2-*e*]tetrazolo[1,5-*a*]pyrimidines; Thiosemicarbazides; Hydrazones.

Introduction

Thienopyrimidine derivatives have received considerable attention due to their wide range of biological activities such as antimicrobial [1, 2], antiviral [3], anticancer [4, 5], anti-inflammatory [6, 7], antihistaminic [8], antipyretics [9], antianaphylactic [10], anticonvulsant [11], and immunostimulant [12] properties. Besides, many thienopyrimidine compounds exhibited analgesic [13], neurotropic [14], molluscicidal and larvicidal [15] activities.

In fact, some of them have been reported to display good activity as Phosphodiesterase [16, 17], dihydrofolate reductase (DHFR) [18], VEGF kinase [19] inhibitors, in addition to prevention of cartilage destruction in articular disease [20, 21]. In continuation of our previous work on searching antiviral compounds [22, 23] and on the title compounds [24], we reported herein the synthesis and structure elucidation of a new series of thienopyrimidine derivatives.

Results and discussion

The starting material ethyl 2-amino-4-isopropylthiophene-3-carboxylate (**1**) is prepared according to the *Gewald* procedure [25]. Its reaction with thiourea or potassium thiocyanate in dioxane gave the corresponding thienopyrimidine **3**. Subsequent methylation with dimethylsulfate and aqueous NaOH afforded 2-methylthio derivative **5** which upon nucleophilic displacement of the S*Me* group with hydrazine furnished the respective hydrazino derivative **7a**. On the other hand, reaction of **3** with two equivalents of methyl iodide gave the corresponding 5-isopropyl-3-methyl-2-(methylthio)thieno[2,3-*d*]-pyrimidin-4-one (**6**) which could be prepared by other route *via* the thiourea **2** followed by cyclization to thienopyrimidine **4**. Subjection of **6** to hydrazine hydrate resulted in the formation of the hydrazino derivative **7b** (Scheme 1). The structure proposal of the prepared compounds was derived from the analytical data (^{1}H NMR, ^{13}C NMR, and IR) and satisfactory elemental analyses.

Dedicated to Prof. Dr. *Erik B. Pedersen* on the occasion of his 63th birthday

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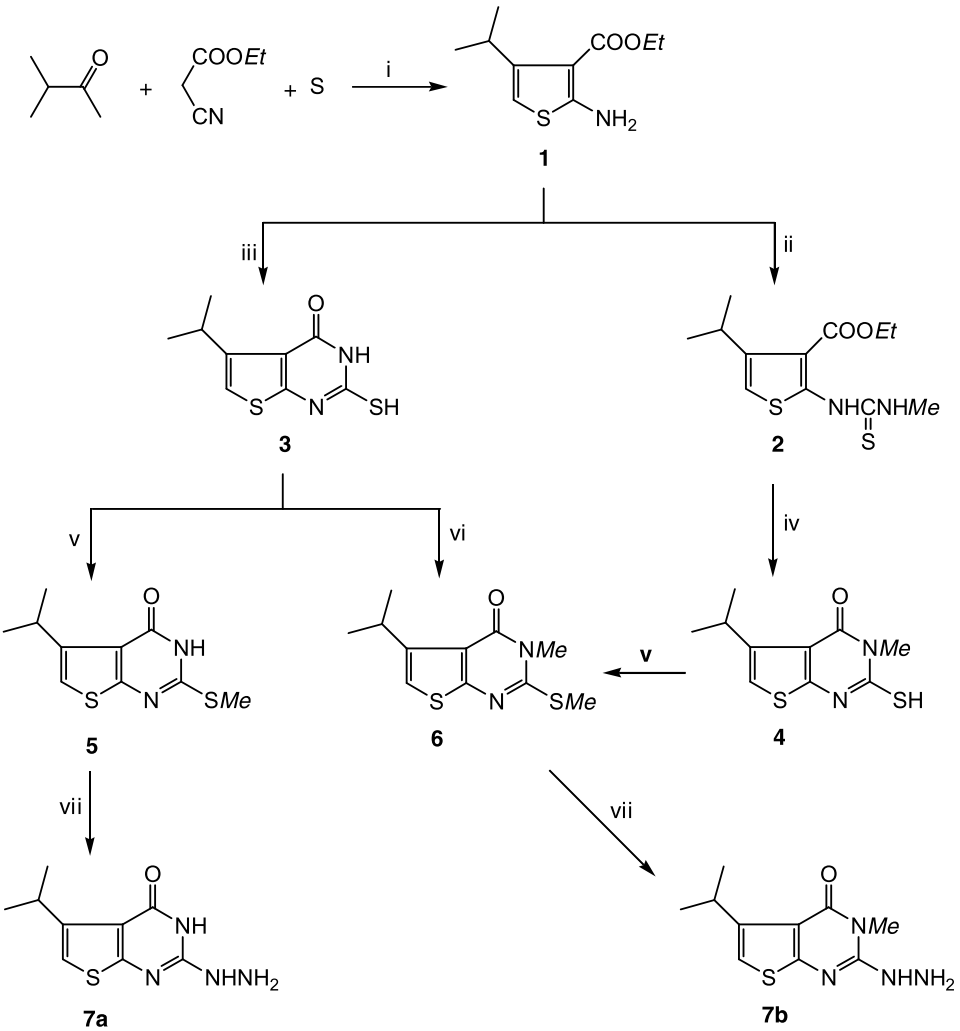


i, morpholin, *Et*OH, 60°C; ii, *Me*NCS, *Et*OH; iii, KSCN, dioxane, *Et*OH; iv, aq. NaOH; v, NaOH, Me_2SO_4; vi, K_2CO_3, acetone, *Me*I; vii, $N_2H_4{\cdot}H_2O$, *Et*OH

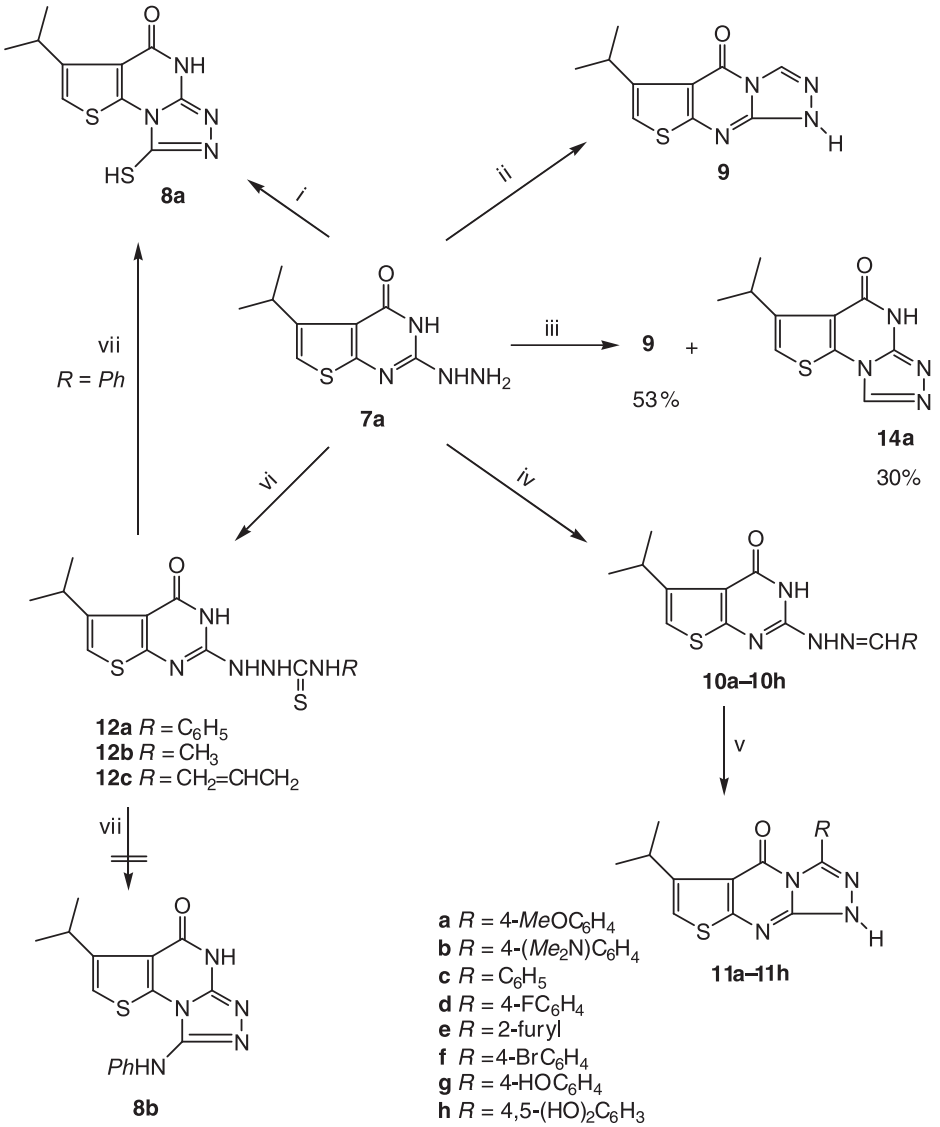
Scheme 1

Synthesis of thieno[2,3-d]triazolo[4,3-a]pyrimidine derivatives

A series of thieno[2,3-*d*]triazolo[4,3-*a*]pyrimidine derivatives was synthesized by condensation of 2-hydrazino-5-isopropylthieno[2,3-*d*]pyrimidin-4-one (**7a**) with various one-carbon doners. For instance, it reacted with formic acid to give the triazolothieno-pyrmidine **9**, whereas with triethylorthoformate a mixture of **9** and its angular isomer **14a** in ratio of 2:1 was obtained. Condensation of **7a** with aromatic aldehydes resulted in the formation of hydrazones **10a**–**10h** in good yields. Oxidative cyclization of the latter compounds by ethanolic ferric chloride solution gave 3-aryl thieno[2,3-*d*]triazolo[4,3-*a*]-pyrimidine derivatives **11a**–**11h** (Scheme 2).

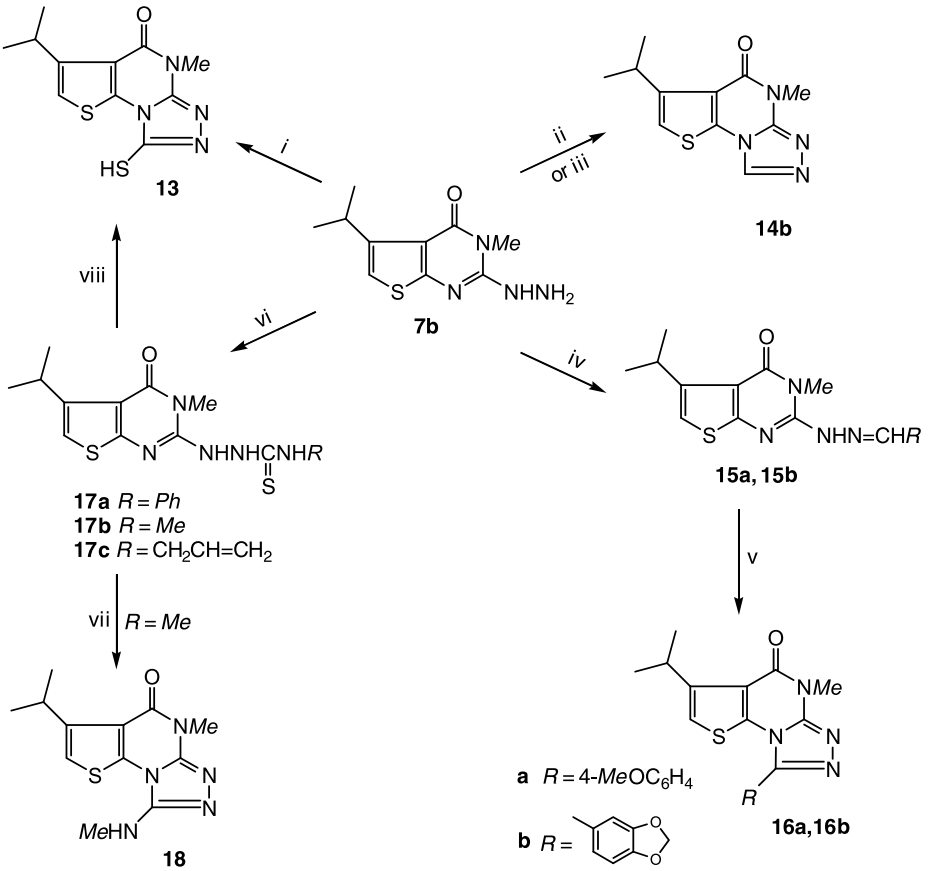
Synthesis of thieno[3,2-e]triazolo[4,3-a]pyrimidine derivatives

Treatment of the hydrazino compound **7b** with formic acid or triethylorthoformate gave exclusively the isomeric product thieno[3,2-*e*]triazolo[4,3-*a*]pyrimidine (**14b**), since N-3 is blocked by methyl group. Condensation of **7b** with aromatic aldehydes furnished the corresponding hydrazones **15a**, **15b**. Dehydrogenative cyclization by ethanolic $FeCl_3$



Scheme 2

solution afforded the triazolothienopyrimidines **16a**, **16b**. Addition of **7b** to alkyl and aryl isothiocyanates resulted in the formation of thiosemicarbazides **17a**–**17c**. Reaction of **17b** with HgO in ethanol gave the expected N-methylamino-triazole **18**, whereas with aqueous NaOH (2M) afforded the mercapto derivative **13**, which could also be obtained by the reaction of **7b** with CS_2 (Scheme 3). The ^{1}H NMR spectra of the hydrazones **15a** and **15b** indicated its existence as a mixture of the *syn*- and *anti*- conformations as indicated by the presence of two doublets for HC=N proton. Aryl and alkyl isothiocyanates reacted with **7a** to provide the corresponding thiosemicarbazides **12a**–**12c** (Scheme 2). Treatment of **12a** with aqueous NaOH (2M) did not give the expected 3-amino derivative **8b**. Instead, the 3-mercapto derivative **8a** was obtained, which could also be prepared by the action of CS_2 on **7a** in pyridine. The IR spectra of [3,2-*e*]thieno[1,2,4]triazolo[4,3-*a*]-pyrimidines **13**, **14**, **16** and **18** (angular structure) showed absorption due to C=O group in the range of $\bar{\nu} = 1651–1680\,\mathrm{cm}^{-1}$. Their ^{1}H NMR spectra displayed resonance for the thiophene proton in the range of $\delta = 7.02–7.18$ ppm. However, the IR spectra of compounds **9** and **11a**–**11h** (linear structure) showed C=O absorption between $\bar{\nu} = 1706$ and

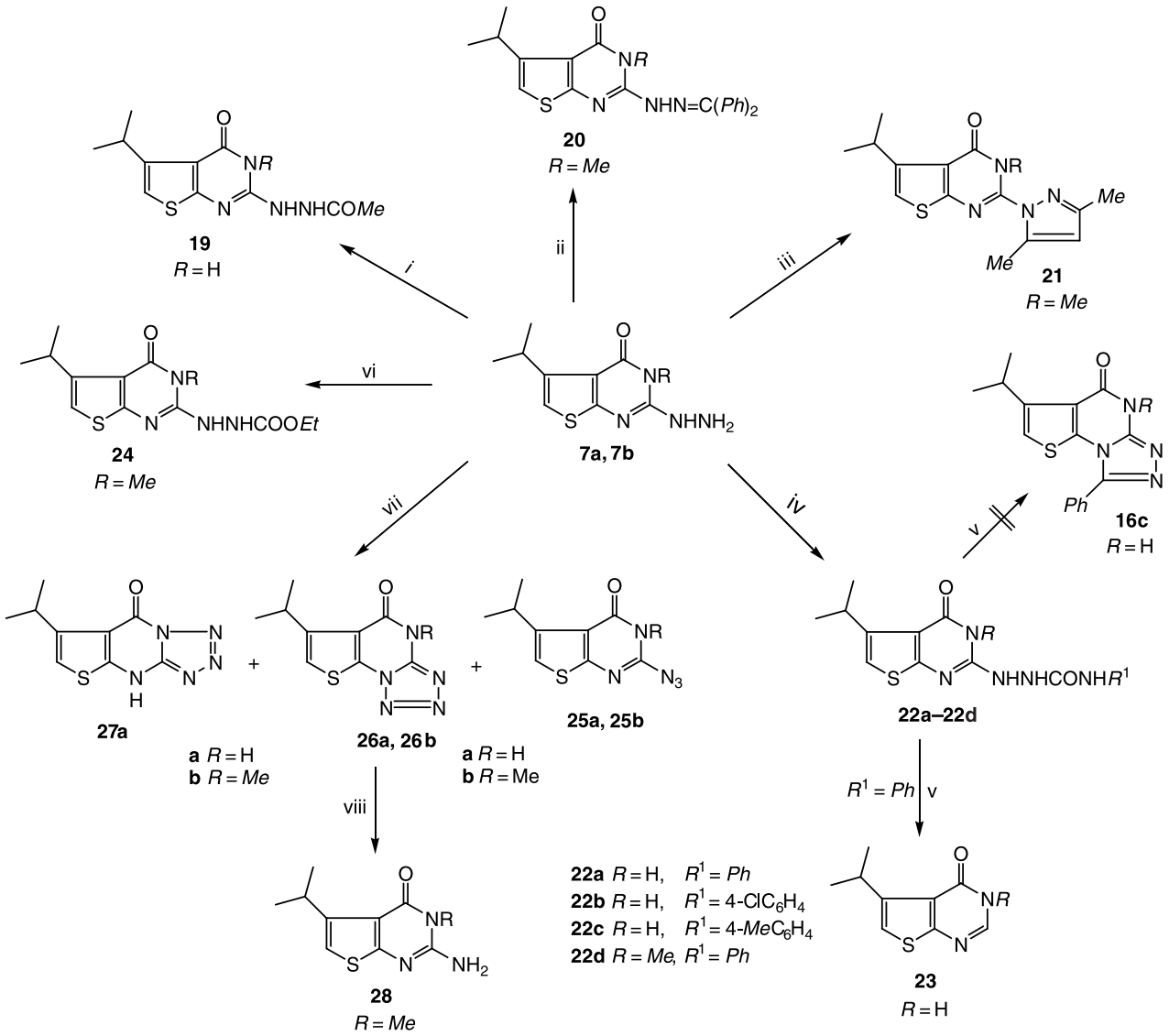


Scheme 3

1713 cm^{-1} and resonance for thiophene proton in ^1H NMR in the range of $\delta = 6.55–6.80$ ppm. Compound **8a** which formed by the action of CS_2 in pyridine on **7a** exhibited in its IR spectrum C=O absorption at $\bar{\nu} = 1675\ cm^{-1}$ and thiophene proton displayed singlet at $\delta = 7.13$ ppm in the ^1H NMR spectrum. Therefore we believe that compound **8a** possess propbably the angular structure 6-isopropyl-3-mercaptothieno[3,2-*e*]triazolo[4,3-*a*]pyrimidin-5-one. Treatment of **7a** with triethylorthoformate afforded the two isomeric products **9** and **14a**, where their thiophene proton displayed resonances in ^1H NMR spectra at $\delta = 6.80$ and 7.16 ppm. The relatively high field region (more deshielded) of thiophene proton in the angular isomer can be attributed to proximity of the triazole ring. This observation could also be seen in ^1H NMR spectra of the tetrazolo compounds **25a**, **25b** where the thiophene proton resonated at $\delta = 7.37$ ppm.

*Miscellaneous reactions of **7a** and **7b** with different reagents*

Compound **7b** reacted with benzophenone to give the hydrazone **20**, while with pentane-2,4-dione, the pyrazolyl derivative **21** was obtained. Addition of arylisocyanate to **7a**, **7b** afforded the corresponding semicarbazides **22a**–**22d**. Treatment of **22a** with aqueous NaOH (2 *M*) did not give the corresponding triazolo derivative **16c**. Instead, 2-unsubstitued thienopyrimidine **23** was formed. Reaction of **7a** with acetic acid furnished the hydrazide **19** wherease with ethyl chloroformate, ethyl-2-(5-isopropyl-3-methyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl) hydrazinecarboxylate **24** was produced. Compound **7a** and **7b** reacted with nitrous acid at 0°C to give the corresponding tetrazolo derivatives **26a** and **26b** and **27a** beside the azido isomer **25a** and **25b** as indicated by ^1H NMR and IR spectra. Treatment of **25b** with Zinc dust in CH_3COOH afforded the corresponding



Scheme 4

2-aminothienopyrimidine **28** (Scheme 4). The constitution of the prepared compounds was secured by their NMR, IR, and MS spectra.

Experimental

Melting points were measured with a *Kofler* Block apparatus. IR spectra were recorded with Perkin – Elmer Model 1720 FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were determined with a varian EM 390 and Bruker AC – 250 spectrometers. The chemical shifts in ppm are expressed in the δ scale using tetramethylsilane as internal standard. Coupling constants are given in Hz. Mass spectra were recorded on an AEIMS 30 spectrometer. TLC was performed on Merck silica gel 60-F 254 precoated plastic plates. Microanalyses were performed in the unit of microanalysis at the universities of Cairo (Egypt) and Odense (Denmark); the results were in satisfactory agreement with the calculated values.

Ethyl-2-amino-4-isopropylthiophene-3-carboxylate
(**1**, $C_{10}H_{15}NO_2S$)

To a stirred mixture of 8.16 g isopropylmethylketone (100 mmol), 11.30 g ethyl cyanoacetate (100 mmol), 9.00 g morpholin (100 mmol) and absolute ethanol 3.00 cm^3, 3.20 g sulfur (100 mmol) was added gradually with continuous stirring in a water bath (60°C) for 6 h. The reaction mixture was cooled and poured into crushed ice (100 cm^3). The sep-

arated solid was filtered off, washed and crystallized from ethanol to give yellow sheets. Yield 12.80 g (60%); mp 52–54°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.13$ (d, 6H, $2CH_3$), 1.27 (t, $J = 7.1$ Hz, 3H, CH_3), 3.34 (m, 1H, H), 4.20 (q, $J = 7.0$ Hz, 2H,CH_2), 5.93 (s, 1H, CH), 7.29 (s, 2H, NH_2) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 14.14$ (CH_3), 23.09 ($2CH_3$), 28.38 (CH), 58.73 (OCH_2), 99.55, 102.81, 146.75, 164.83 (thiophene), 165.52 (C=O) ppm.

Ethyl-4-isopropyl-2-(3-methylthiourenyl)-3-carboxylate (**2**, $C_{12}H_{18}N_2O_2S_2$)

A mixture of 2.13 g **1** (10 mmol) and 0.73 g methyl isothiocyanate (10 mmol) in 10 cm^3 absolute ethanol, was boiled under reflux for 3 h. The reaction mixture was cooled and poured onto cold water. The separated solid was filtered off, washed with H_2O, dried and crystallized from ethanol to give brown crystals. Yield 2.03 g (71%); mp 118–120°C; IR (KBr): $\bar{\nu} = 1574$ (C=C), 1639 (C=O), 3243 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.12$ (m, 9H, CH_3), 1.33 (d, 3H, NCH_3), 2.91 (q, 2H, CH_2), 4.30 (m, 1H, CH), 6.52 (s, 1H, CH), 9.40, 11.51 (2bs, 2H, 2NH) ppm.

5-Isopropyl-2-mercaptothieno[2,3-d]pyrimidin-4(3H)-one (**3**, $C_9H_{10}N_2OS_2$)

A mixture of 4.26 g **1** (20 mmol) and excess of potassium thiocyanate (3.88 g, 40 mmol) in 25 cm^3 dioxan and 5 cm^3 absolute ethanol was stirred with gradually addition of 5 cm^3 hydrochloric acid 37%. The reaction mixture was boiled under reflux for 6 h. Then, it was cooled and poured into cold water. The separated solid was boiled in sodium hydroxide (1 *M*, 50 cm^3) for 10 min, then cooled and neutralized by addition of 1 *M* hydrochloric acid. The precipitate was filtered off, washed, and crystallized from ethanol as colorless crystals. Yield 2.26 g (50%); mp 52–54°C; IR (KBr): $\bar{\nu} = 1536$ (C=C), 1671 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.18$ (d, 6H, $2CH_3$), 3.46 (m, 1H, CH), 6.88 (s, 1H, CH), 12.34, 13.44 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.62$ ($2CH_3$), 27.85 (CH), 11.37, 115.90, 145.59, 152.83 (thiophene), 156.89 (C=O), 172.95 (C=S) ppm.

5-Isopropyl-2-mercapto-3-methylthieno[2,3-d]pyrimidin-4-one (**4**, $C_{10}H_{12}N_2OS_2$)

A solution of 2.86 g **2** (10 mmol) in 15 cm^3 2 *M* sodium hydroxide was boiled under reflux for 1 h. After cooling the reaction mixture was neutralized by 2 *M* hydrochloric acid. The precipitate was filtered off, dried, and crystallized from ethanol as white crystals. Yield 1.39 g (67%); mp 178–180°C; IR (KBr): $\bar{\nu} = 1266$ (C=S), 1543 (C=C), 1568 (C=N), 1693 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.20$ (d, 6H, $2CH_3$), 3.33 (s, 3H, NCH_3), 3.53 (m, 1H, CH), 6.90 (s, 1H, CH), 13.64 (s, 1H, SH) ppm.

5-Isopropyl-2-(methylthio)thieno[2,3-d]pyrimidin-4(3H)-one (**5**, $C_{10}H_{12}N_2OS_2$)

A solution of 3.39 g **3** (15 mmol) in 150 cm^3 0.1 *M* sodium hydroxide and 15 cm^3 dimethylsulfate was stirred for 5 min. The precipitated solid was dissolved by addition of 4 *M* sodium hydroxide and the solution was heated at 70°C for 10 min. After cooling, the solution was filtered and neutralized by 2 *M* hydrochloric acid. The precipitate was filtered off, dried, and recrystallized from ethanol as brown crystals. Yield 2.88 g (80%); mp 178–180°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.23$ (d, 6H, $2CH_3$), 2.49 (s, 3H, SCH_3), 3.55 (m, 1H, CH), 7.00 (s, 1H, CH), 12.51 (bs, 1H, NH) ppm.

5-Isopropyl-3-methyl-2-(methylthio)thieno[2,3-d]pyrimidin-4-one (**6**, $C_{11}H_{14}N_2OS_2$)

Method A: A mixture of 2.26 g **3** (10 mmol) and 2.76 g potassium carbonate (20 mmol) in 50 cm^3 dry acetone was stirred for 2 h. Methyliodid (2.84 g, 20 mmol) was added gradually with stirring over night. The reaction mixture was filtered and the solvent was evaporated under vacuum. The solid residue was washed and crystallized from ethanol as brown crystals. Yield 1.39 g (67%); mp 178–180°C; IR (KBr): $\bar{\nu} = 1561$ (C=C, C=N), 1667 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 2.57 (s, 3H, SCH_3), 3.45 (s, 3H, NCH_3), 3.61 (m, 1H, CH), 6.99 (s, 1H, CH) ppm.

Method B: A mixture of 2.08 g **4** (10 mmol) and 1.38 g potassium carbonate (10 mmol) in 50 cm^3 dry acetone was stirred for 1 h. Methyliodide (1.42 g, 10 mmol) was added gradually. Working up as described before afforded brown crystals. Yield 1.45 (70%).

2-Hydrazino-5-isopropylthieno[2,3-d]pyrimidin-4(3H)-one (**7a**, $C_9H_{12}N_4OS$)

A mixture of 0.24 g **5** (1 mmol) and 5 cm^3 $NH_2NH_2 \cdot H_2O$ in 15 cm^3 absolute ethanol was boiled under reflux for 3 h. The colorless product that separated on cooling was filtered off and recrystallized from ethanol to provide colorless crystals. Yield 0.15 g (70%); mp 244–246°C; IR (KBr): $\bar{\nu} = 1614$ (C=C, C=N), 1778 (C=O), 3264 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 3.47 (m, 1H, CH), 4.80 (bs, 2H, NH_2), 6.58 (s, 1H, CH) 8.29, (bs, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.72$ ($2CH_3$), 28.23 (CH), 107.70, 113.16, 145.07, 154.62 (thiophene), 157.80, (C=N), 168.72 (C=O) ppm.

2-Hydrazino-5-isopropyl-3-methylthieno[2,3-d]pyrimidin-4-one (**7b**, $C_{10}H_{14}N_4OS$)

From 0.22 g **6** (1 mmol) and hydrazine hydrate as described for **7a** to give colorless crystyals. Yield 0.17 g (72%); mp 250–252°C; IR (KBr): $\bar{\nu} = 1530$ (C=C, C=N), 1675 (C=O) 3210 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.20$ (d, 6H, $2CH_3$), 3.29 (s, 1H, CH_3), 3.50 (m, 1H, CH), 4.42 (bs, 2H, NH_2) 6.62 (s, 1H, CH), 8.23 (bs, 1H, NH) ppm.

6-Isopropyl-3-mercaptothieno[3,2-e][1,2,4]triazolo[4,3-a]-pyrimidin-5(1H)-one (**8**, $C_{10}H_{10}N_4OS_2$)

Method A: A mixture of 2.24 g **7a** (10 mmol) and 0.91 g CS_2 (12 mmol) in 15 cm^3 pyridine was heated under reflux for 6 h and then allowed to cool. The solid product was washed and recrystallized from ethanol to give white powder. Yield 1.86 g (70%); mp 282–284°C; IR (KBr): $\bar{\nu} = 1647$ (C=C, C=N), 1676 (C=O), 3118 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.25$ (s, 6H, $2CH_3$), 3.72 (m, 1H, CH), 7.15 (s, 1H, CH), 12.54, 13.83 (2bs, 2H, 2NH) ppm; ^{13}C NMR $\delta = 23.01$ ($2CH_3$), 27.16 (CH),

114.51, 117.30, 142.04, 145.35 (thiophene), 149.49 (C=N), 157.18 (C=O), 158.50 (C=S) ppm.

Method B: A solution of 0.36 g **12a** (1 mmol) and 25 cm^3 2 *M* sodium hydroxide was boiled for 20 min and then neutralized by addition of 2 *M* hydrochloric acid. The precipitate formed was collected, washed and crystallized from ethanol as white crystals. Yield 0.19 g (71%).

6-Isopropylthieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one (**9**, $C_{10}H_{10}N_4OS$)

Method A: A solution of 2.24 g **7a** (10 mmol) in 10 cm^3 formic acid was heated under reflux for 8 h. The reaction mixture was allowed to cool and then poured onto 100 cm^3 ice cold water. The separated product was filtered off, washed with water, dried, and crystallized from ethanol as colorless crystals. Yield 1.63 g (70%); mp 203–205°C; IR (KBr): $\bar{\nu} = 1620$ (C=C, C=N), 1704 (C=O), 3097 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.25$ (d, 6H, $2CH_3$), 3.58 (m, 1H, CH), 6.80 (s, 1H, CH), 9.08 (s, 1H, N=CH), 13.84 (bs, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.69$ ($2CH_3$), 28.47 (CH), 109.68, 111.09, 144.64, 148.47 (thiophene), 131.96, 151.49 (2C=N), 169.74 (C=O) ppm.

Method B: A solution of 0.67 g **7a** (3 mmol) in 20 cm^3 triethyl orthoformate was boiled under reflux for 4 h. The reaction mixture showed two spots on TLC plate using 2% CH_2Cl_2/*Me*OH as eluent. A solid product was precipitated on hot and filtered off as white powder (**14a**). Evaporating of the solvent from the mother liquor, washing the solid residue, and crystallization from methylene chloride afforded pale green crystals. Yield 0.38 g (53%).

*General procedure for the synthesis of compounds **10a–10h***

A solution of 10 mmol **7a** and 10 mmol appropriate aromatic aldehyde in 30 cm^3 ethanol containing a few drops of glacial acetic acid, was boiled under reflux for 3 h. The product that separated on cooling was filtered off, dried, and crystallized from ethanol.

4-Methoxybenzaldehyde (5-isopropyl-4-oxo-3,4-dihydro-thieno[2,3-d]pyrimidine-2-yl)hydrazone (**10a**, $C_{17}H_{18}N_4O_2S$)

From 2.24 g **7a** (10 mmol) and 1.36 g *p*-anisaldehyde (10 mmol) as described before. Yield 2.56 g (75%) as yellow crystals; mp 208–211°C; IR (KBr): $\bar{\nu} = 1591$ (C=C, C=N), 1662 (C=O), 3164, 3353 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.10$ (d, 6H, $2CH_3$), 3.40 (m, 1H, CH), 3.67 (s, 3H, OCH_3), 6.54 (s, 1H, CH), 6.84 (d, $J = 8.5$ Hz, 2H, *Ar*–H), 7.74 (d, $J = 8.4$ Hz, 2H, *Ar*–H), 7.86 (s, 1H, N=CH), 11.07, 11.42 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.79$ (2*Me*), 28.27 (CH), 55.19 (O*Me*), 109.08, 114.59, 145.39, 150.10 (thiophene), 113.92, 126.85, 128.96, 143.05 (*Ar*–C), 158.22, 160.43 (2C=N), 167.95 (C=O) ppm.

4-(Dimethylamino)benzaldehyde (5-isopropyl-4-oxo-3,4-dihydrothieno[2,3-d] pyrimidine-2-yl)hydrazone (**10b**, $C_{18}H_{21}N_5OS$)

From **7a** and 1.49 g 4-(dimethylamino)benzaldehyde (10 mmol). Yield 2.84 g (80%) as yellow crystals; mp 247–249°C; IR (KBr): $\bar{\nu} = 1590$ (C=C, C=N), 1661 (C=O), 3227, 3365 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 2.97 (s, 6H, $2CH_3$), 3.53 (m, 1H, CH), 6.66 (s, 1H, CH), 6.73 (d, $J = 9.8$ Hz, 2H, *Ar*–H), 7.71 (d, $J = 9.0$ Hz, 2H, *Ar*–H), 7.93 (s, 1H, N=CH), 10.97, 11.42 (2s, 2H, 2NH) ppm; ^{13}CNMR (*DMSO*-d_6): $\delta = 22.50$ (2Me), 27.98 (CH), 39.44 ($2CH_3$), 108.46, 113.97, 143.86, 145.08 (thiophene), 111.23, 121.33, 128.34, 149.79 (*Ar*–C), 150.87, 157.84 (2C=N), 167.88 (C=O) ppm.

Benzaldehyde (5-isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]-pyrimidine-2-yl)hydrazone (**10c**, $C_{16}H_{16}N_4OS$)

From **7a** and 1.06 g benzaldehyde (10 mmol). Yield 2.34 (75%) as yellow crystals; mp 250–252°C; IR (KBr): $\bar{\nu} =$ 1610 (C=C, C=N), 1656 (C=O), 3153 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.24$ (d, 6H, $2CH_3$), 3.55 (m, 1H, CH), 6.72 (s, 1H, CH), 7.40, 7.95 (m, 5H, *Ar*–H), 8.06 (s, 1H, N=CH), 11.17, 11.60 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.78$ ($2CH_3$), 28.26 (CH), 109.37, 114.85, 143.08, 145.40 (thiophene), 127.32, 128.40, 129.46, 134.17 (*Ar*–C), 150.03, 158.21 (2C=N), 167.76 (C=O) ppm.

4-Fluorobenzaldehyde (5-isopropyl-4-oxo-3,4-dihydro-thieno-[2,3-d]pyrimidine-2-yl)hydrazone (**10d**, $C_{16}H_{15}FN_4OS$)

From **7a** and 1.24 g 4-fluorobenzaldehyde (10 mmol). Yield 2.44 g (74%) as colorless crystals; mp 269–271°C; IR (KBr): $\bar{\nu} = 1608$ (C=C, C=N), 1663 (C=O), 3282 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.09$ (d, 6H, $2CH_3$), 3.40 (m, 1H, CH), 6.55 (s, 1H, CH), 7.10 (d, $J = 8.7$ Hz, 2H, *Ar*–H), 7.87 (d, $J = 2.1$ Hz, 2H, *Ar*–H), 7.90 (s, 1H, N=CH), 11.27, 11.54 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.78$ ($2CH_3$), 28.26 (CH), 109.33, 114.85, 145.40, 150.06 (thiophene), 115.24, 129.59, 130.87, 141.88 (*Ar*–C), 158.28, 161.17 (2C=N), 167.76 (C=O) ppm.

2-Fluraldehyde (5-isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-2-yl)hydrazone (**10e**, $C_{14}H_{14}N_4O_2S$)

From **7a** and 0.96 g 2-furaldehyde (10 mmol). Yield 2.02 (67%) as pale brown crystals; mp 246–248°C; IR (KBr): $\bar{\nu} = 1612$ (C=C, C=N), 1654 (C=O), 3396, 3569 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.24$ (d, 6H, $2CH_3$), 3.53 (m, 1H, CH), 6.64 (s, 1H, CH), 6.72 (s, 1H, *Ar*–H), 7.10 (d, 1H, *Ar*–H), 7.82 (s, 1H, *Ar*–H), 7.98 (s, 1H, N=CH), 10.64, 11.70 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.77$ ($2CH_3$), 28.26 (CH), 109.60, 114.90, 145.36, 149.95 (thiophene), 111.94, 112.19, 133.18, 144.60 (Furan), 150.00, 157.75 (2C=N), 167.75 (C=O) ppm.

4-Bromobenzaldehyde (5-isopropyl-4-oxo-3,4-dihydrothieno-[2,3-d]pyrimidine-2-yl)hydrazone (**10f**, $C_{16}H_{15}BrN_4OS$)

From **7a** and 1.85 g 4-bromobenzaldehyde (10 mmol). Yield 3.04 (78%) as yellow crystals; mp 295–297°C; IR (KBr): $\bar{\nu} = 1599$ (C=C, C=N), 1662 (C=O), 3156, 3347 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.24$ (d, 6H, $2CH_3$), 3.55 (m, 1H, CH), 6.72 (s, 1H, CH), 7.62 (d, $J = 8.4$ Hz, 2H, *Ar*–H), 7.93 (d, $J = 8.6$ Hz, 2H, *Ar*–H), 8.02 (s, 1H, N=CH), 11.46, 11.76 (2s, 2H, 2NH); ^{13}C NMR (*DMSO*-d_6): $\delta =$ 22.79 ($2CH_3$), 28.26 (CH), 109.49, 114.98, 141.75, 145.41

(thiophene), 122.68, 129.24, 131.34, 133.53 (*Ar*–C), 149.96, 158.28 (2C=N), 167.65 (C=O) ppm.

4-Hydroxybenzaldehyde (5-isopropyl-4-oxo-3,4-dihydro-thieno[2,3-d]pyrimidine-2-yl)hydrazone (**10g**, $C_{16}H_{16}N_4O_2S$)
From **7a** and 1.22 g 4-hydroxybenzaldehyde (10 mmol). Yield 2.42 (74%) as colorless crystals; mp 277–279°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.24$ (d, 6H, $2CH_3$), 3.55 (m, 1H, CH), 6.67 (s, 1H, CH), 6.83 (d, $J = 8.7$ Hz, 2H, *Ar*–H), 7.76 (d, $J = 8.7$ Hz, 2H, *Ar*–H), 7.97 (s, 1H, N=CH), 9.85 (bs, 1H, OH), 11.11, 11.53 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.78$ ($2CH_3$), 28.27 (CH), 108.94, 114.48, 145.39, 150.11 (thiophene), 115.33, 125.36, 129.09, 143.52 (*Ar*–C), 158.17, 159.00 (2C=N), 168.03 (C=O) ppm.

3,4-Dihydroxybenzaldehyde (5-isopropyl-4-oxo-3,4-dihydro-thieno[2,3-d]pyrimidine-2-yl)hydrazone (**10h**, $C_{16}H_{16}N_4O_3S$)
From **7a** and 1.38 g 3,4-dihydroxybenzaldehyde (10 mmol). Yield 2.44 (71%) as colorless crystals; mp 273–275°C; IR (KBr): $\bar{\nu} = 1578$ (C=C, C=N), 1632 (C=O), 3318, 3413 (NH), 3651 (OH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.24$ (d, 6H, $2CH_3$), 3.54 (m, 1H, CH), 6.68 (s, 1H, CH), 6.79, 7.10 (2d, 2H, *Ar*–H), 7.40 (s, 1H, *Ar*–H), 7.90 (s, 1H, N=CH), 9.10, 9.40 (2bs, 2H, 2OH), 10.89, 11.46 (2s, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.79$ (2*Me*), 28.27 (CH), 109.01, 114.48, 145.46, 147.53 (thiophene), 113.65, 115.30, 120.28, 125.68, 143.94, 145.36 (*Ar*–C), 150.04, 158.03 (2C=N), 168.08 (C=O) ppm.

*General procedure for the synthesis of compounds **11a–11h***
A solution of 0.4 g ferric chloride in 5 cm^3 ethanol was added dropewise to a boiling solution of 2 mmol aldehyde hydrazones **10a**–**10h** in 50 cm^3 ethanol. Heating was continued for 30 min and the mixture was then kept overnight at room temperature. Evaporation of the solvent under reduced pressure, washing the residue with water, and drying afforded a solid product which could be crystallized from ethanol.

6-Isopropyl-3-(4-methoxyphenyl)thieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one (**11a**, $C_{17}H_{16}N_4O_2S$)
From 0.68 g **10a** (2 mmol) and $FeCl_3$ as described before. Yield 0.47 g (70%) as colorless crystals; mp 223–225°C; IR (KBr): $\bar{\nu} = 1624$ (C=C, C=N), 1713 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.53 (m, 1H, CH), 3.85 (s, 3H, OCH_3), 6.77 (s, 1H, CH), 7.07, 7.66 (2d, 4H, *Ar*–H), 14.15 (s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.80$ (2*Me*), 28.38 (CH), 55.24 (OCH_3), 109.38, 111.47, 144.40, 145.07 (thiophene), 112.84, 119.51, 124.22, 131.88 (*Ar*–C), 149.63, 152.78 (C=N), 160.42 (C=O) ppm.

3-[4-(Dimethylamino)phenyl]-6-isopropylthieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one (**11b**, $C_{18}H_{19}N_5OS$)
From 0.71 g **10b** (2 mmol) and $FeCl_3$. Yield (0.44 g, 63%) as green crystals; mp 215–217°C; IR (KBr): $\bar{\nu} = 1611$ (C=C, C=N), 1708 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 3.00 (s, 6H, $N(CH_3)2$), 3.54 (m, 1H, CH), 6.74 (s, 1H, CH), 6.76, 7.56 (m, 4H, *Ar*–H), 14.00 (s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.79$ ($2CH_3$), 28.37 (CH), 39.76 ($2NCH_3$), 109.17, 111.36, 145.06, 145.18 (thiophene), 110.44, 114.03, 131.24, 149.64 (*Ar*–C), 150.99, 152.85 (2C=N), 168.82 (C=O) ppm.

6-Isopropyl-3-phenylthieno[2,3-d][1,2,4]triazolo[4,3-a]-pyrimidin-5(1H)-one (**11c**, $C_{16}H_{14}N_4OS$)
From 0.62 g **10c** (2 mmol) and $FeCl_3$. Yield 0.37 g (60%) as brown powder; mp 180–182°C; IR (KBr): $\bar{\nu} = 1626$ (C=C, C=N), 1709 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.09$ (d, 6H, $2CH_3$), 3.40 (bm, 1H, CH), 6.55 (s, 1H, CH), 7.10, 7.90 (m, 5H, *Ar*–H), 12.55 (bs, 1H, NH) ppm; $m/z = 310$ (M^+).

3-(4-Fluorophenyl)-6-isopropylthieno[2,3-d][1,2,4]triazolo-[4,3-a]pyrimidin-5(1H)-one (**11d**, $C_{16}H_{13}F\ N_4OS$)
From 0.66 g **10d** (2 mmol) and $FeCl_3$. Yield 0.42 g (65%) as brownish yellow powder; mp 215–217°C; IR (KBr): $\bar{\nu} = 1613$ (C=C, C=N), 1709 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.20$ (d, 6H, $2CH_3$), 3.69 (m, 1H, CH), 6.76 (s, 1H, CH), 7.34, 7.80 (m, 4H, *Ar*–H), 12.75 (bs, 1H, NH) ppm.

3-(2-Furyl)-6-isopropylthieno[2,3-d][1,2,4]triazolo[4,3-a]-pyrimidin-5(1H)-one (**11e**, $C_{14}H_{12}N_4O_2S$)
From 0.60 g **10e** (2 mmol) and $FeCl_3$. Yield 0.34 g (67%) as brown crystals; mp 235–237°C; IR (KBr): $\bar{\nu} = 1624$ (C=C, C=N), 1712 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.25$ (d, 6H, $2CH_3$), 3.58 (m, 1H, CH), 6.71 (s, 1H, CH), 6.80 (d, 1H, *Ar*–H), 7.46 (d, 1H, *Ar*–H), 7.95 (s, 1H, *Ar*–H), 14.25 (s, 1H, NH) ppm; $m/z = 300$ (M^+).

3-(4-Bromophenyl)-6-isopropylthieno[2,3-d][1,2,4]triazolo-[4,3-a]pyrimidin-5(1H)-one (**11f**, $C_{16}H_{13}BrN_4OS$)
From 0.78 g **10f** (2 mmol) and $FeCl_3$. Yield 0.50 g (65%) as pale yellow crystals; mp 228–230°C; IR (KBr): $\bar{\nu} = 1622$ (C=C, C=N), 1710 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 3.68 (bm, 1H, CH), 6.78 (bs, 1H, CH), 7.00, 7.70 (m, 4H, *Ar*–H), 12.80 (bs, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.37$ ($2CH_3$), 27.85 (CH), 108.98, 113.21, 142.91, 145.29 (thiophene), 123.05, 126.03, 129.95, 131.87 (*Ar*–C), 149.40, 151.94 (2C=N), 167.50 (C=O) ppm.

3-(4-Hydroxyphenyl)-6-isopropylthieno[2,3-d][1,2,4]triazolo-[4,3-a]pyrimidin-5(1H)-one (**11g**, $C_{16}H_{14}N_4O_2S$)
From 0.66 g **10g** (2 mmol) and $FeCl_3$. Yield 0.39 g (60%) as white powder; mp 248–250°C; IR (KBr): $\bar{\nu} = 1614$ (C=C, C=N), 1685 (C=O), 3107 (NH), 3326 (OH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.20$ (d, 6H, $2CH_3$), 3.51 (m, 1H, CH), 6.61 (s, 1H, CH), 6.83, 7.60 (m, 4H, *Ar*–H), 9.90 (bs, 1H, OH), 14.00 (bs, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.69$ ($2CH_3$), 28.23 (CH), 108.85, 111.06, 144.89, 150.11 (thiophene), 114.05, 118.00, 131.77, 143.50 (*Ar*–C), 152.50, 158.75 (2C=N), 168.59 (C=O) ppm; $m/z = 326$ (M^+).

3-(3,4-Dihydroxyphenyl)-6-isopropylthieno[2,3-d][1,2,4]-triazolo[4,3-a]pyrimidin-5(1H)-one (**11h**, $C_{16}H_{12}N_4O_3S$)
From 0.69 g **11h** (2 mmol) and $FeCl_3$. Yield 0.42 g (61%) as brown powder; mp >300°C; IR (KBr): $\bar{\nu} = 1609$ (C=C, C=N), 1694 (C=O), 3350 (OH) cm^{-1}.

*General procedure for the synthesis of compounds **12a–12c***
A solution of 0.22 g **7a** (1 mmol) and an excess of isothiocyanate (2.5 mmol) in 10 cm^3 ethanol was boiled under reflux for 4 h. The product that separated on cooling was filtered off, and recrystallized from ethanol.

2-(5-Isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)-N-phenylhydrazine carbothioamide (**12a**, $C_{16}H_{17}N_5OS_2$)
From **7a** and 0.30 g phenyl isothiocyanate (2.5 mmol). Yield 0.27 g (75%) as colorless crystals; mp 270–272°C; IR (KBr): $\bar{\nu} = 1608$ (C=C, C=N), 1659 (C=O), 3170, 3280 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.49 (m, 1H, CH), 6.74 (s, 1H, CH), 7.14 (m, 1H, *Ar*–H), 7.32 (m, 2H, *Ar*–H), 7.35 (m, 2H, *Ar*–H), 8.66, 9.58, 9.85, 11.15 (4s, 4H, 4NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.80$ ($2CH_3$), 28.27 (CH), 109.94, 115.24, 145.19, 152.34 (thiophene), 124.84, 128.04, 139.05 (*Ar*–C), 158.29 (C=N), 167.78 (C=O), 181.61 (C=S) ppm.

2-(5-Isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)-N-methylhydrazine carbothioamide (**12b**, $C_{11}H_{15}N_5OS_2$)
From **7a** and 0.18 g methyl isothiocyanate (2.5 mmol). Yield 0.22 g (74%) as pale yellow crystals; mp 202–204°C; IR (KBr) $\bar{\nu} = 1609$ (C=C, C=N), 1664 (C=O), 3168, 3304 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 2.88 (d, 3H, NCH_3), 3.50 (m, 1H, CH), 6.73 (s, 1H, CH), 8.13 (m, 1H, NH), 8.47, 9.21, 11.00 (3s, 3H, 3NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.73$ ($2CH_3$), 28.20 (CH), 30.82 (N–CH_3), 109.79, 115.21, 145.10, 152.50 (thiophene), 157.85 (C=N), 167.88 (C=O), 182.50 (C=S) ppm.

N-Allyl-2-(5-isopropyl-4-oxo-3,4dihydrothieno[2,3-d]-pyrimidin-2-yl)hydrazine carbothioamid (**12c**, $C_{13}H_{17}N_5OS_2$)
From **7a** and 0.25 g allyl isothiocyanate (2.5 mmol). Yield 0.23 g (71%) as yellow crystals; mp 170–172°C; IR (KBr): $\bar{\nu} = 1606$ (C=C, C=N), 1665 (C=O), 3160, 3289 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 3.51 (m, 1H, CH), 4.10 (d, 2H, CH_2), 5.05 (q, 2H, N–CH_2), 5.81 (m, 1H, CH), 6.73 (s, 1H, CH), 8.33, 8.50, 9.30, 11.00 (4s, 4H, 4NH) ppm.

3-Isopropyl-8-mercapto-5-methylthieno[3,2-e][1,2,4]-triazolo-[4,3-a]pyrimidin-4(5H)-one (**13**, $C_{13}H_{14}N_2OS_2$)
From 2.38 g **7b** (10 mmol) and 0.91 g CS_2 (12 mmol) in 15 cm^3 pyridine, Yield 2.04 g (73%); mp 257–259°C; IR (KBr): $\bar{\nu} = 1615$ (C=C, C=N), 1651 (C=O), 3202 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.24$ (d, 6H, $2CH_3$), 3.39 (s, 3H, NCH_3), 3.72 (m, 1H, CH), 7.15 (s, 1H, CH), 14.09 (s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 23.00$ ($2CH_3$), 27.21 (CH), 27.90 (N–CH_3), 114.69, 116.73, 141.11, 145.30 (thiophene), 156.04 (C=N), 159.39 (C=O), 162.02 (C=S) ppm.

3-Isopropylthieno[3,2-e]triazolo[4,3-a]pyrimidin-4(5H)-one (**14a**, $C_{10}H_{10}N_4OS$)
A solution of 2.24 g **7a** (10 mmol) in 10 cm^3 triethyl orthoformate was heated under reflux for 4 h. A solid was precipitated on hot which was filtered off, washed with methylenechloride, and crystallized from ethanol to give white crystals. Yield 0.38 g (53%); mp 258–260°C; IR (KBr): $\bar{\nu} = 1625$ (C=C, C=N), 1692 (C=O), 3104 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.25$ (d, 6H, $2CH_3$), 3.68 (m, 1H, CH), 7.16 (s, 1H, CH), 9.18 (s, 1H, N=CH), 12.71 (bs, 1H, NH) ppm.

3-Isopropyl-5-methylthieno[3,2-e]triazolo[4,3-a]pyrimidin-4-one (**14b**, $C_{11}H_{12}N_4OS$)
Method A: A solution of 0.24 g **7b** (1 mmol) in 10 cm^3 formic acid was heated under reflux for 8 h. The reaction mixture was allowed to cool and poured onto 100 cm^3 ice cold water. The separated product was filtered off, washed with water, dried, and crystallized from ethanol as colorless crystals. Yield 0.17 g (70%); mp 160–162°C; IR (KBr): $\bar{\nu} = 1600$ (C=C, C=N), 1671 (C=O), 3097 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.25$ (d, 6H, $2CH_3$), 3.56 (s, 3H, NCH_3), 3.69 (m, 1H, CH), 7.17 (s, 1H, CH), 9.21 (s, 1H, N=CH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.82$ ($2CH_3$), 27.78 (CH), 113.78, 116.61, 141.64, 148.23 (thiophene), 135.69, 155.49 (2C=N), 169.74 (C=O).

Method B: A solution of 0.24 g **7b** (1 mmol) in 10 cm^3 triethyl orthoformate was boiled under reflux for 4 h. After cooling the reaction mixture was poured into ice water. The separated product was filtered off, washed, dried, and crystallized from ethanol.

*General procedure for the synthesis of compounds **15a** and **15b***
A solution of 2.38 g **7b** (10 mmol) and 10 mmol appropriate aromatic aldehyde in 30 cm^3 ethanol containing a few drops of glacial acetic acid, was boiled under reflux for 3 h. The product that separated on cooling was filtered off, dried, and crystallized from ethanol.

4-Methoxybenzaldehyde (5-isopropyl-3-methyl-4-oxo-dihydrothieno[2,3-d]pyrimidin-2-yl) hydrazone (**15a**, $C_{18}H_{20}N_4O_2S$)
From **7b** and 1.36 g 4-methoxybenzaldehyde (10 mmol). Yield 2.63 g (74%) as orange crystals; mp 115–117°C; IR (KBr): $\bar{\nu} = 1608$ (C=C, C=N), 1665 (C=O), 3222 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.20$ (d, 6H, $2CH_3$), 3.33 (s, 3H, NCH_3), 3.49 (m, 1H, CH), 3.81 (s, 3H, OCH_3), 7.00 (s, 1H, CH), 7.65, 7.87 (2d, 4H, *Ar*–H), 8.31 (d, 1H, CH), 1.61 (s, 2H, 2NH) ppm.

1,3-Benzodioxole-5-carbaldehyde (5-isopropyl-3-methyl-4-oxo-3,4-dihydrothieno[2,3-d] pyrimidin-2-yl)hydrazone (**15b**, $C_{18}H_{18}N_4O_3S$)
From 2.38 g **7b** (10 mmol) and 1.50 g 1,3-benzodioxole-5-carbaldehyde (10 mmol). Yield 2.74 g (74%) as orange crystals; mp 110–112°C; IR (KBr): $\bar{\nu} = 1601$ (C=C, C=N), 1675 (C=O), 3240 (NH) cm^{-1}.

*General procedure for the synthesis of compounds **16a** and **16b***
A solution of 0.4 g ferric chloride in 5 cm^3 ethanol was added dropwise to a boiling solution of 2 mmol aldehyde hydrazone **15** in 30 cm^3 ethanol. Heating was continued for 30 min and the mixture was then kept overnight at room temperature. Evaporation of the solvent under reduced pressure, washing with water, and drying afforded a solid product which could be crystallized from ethanol.

3-Isopropyl-8-(4-methoxyphenyl)-5-methylthieno[3,2-e]-[1,2,4]triazolo[4,3-a]pyrimidin-4-one (**16a**, $C_{18}H_{18}N_4O_2S$)
From 0.71 g **15a** (2 mmol) and $FeCl_3$ as described before. Yield 0.51 g (72%) as brown powder; mp 178–180°C; IR (KBr): $\bar{\nu} = 1594$ (C=C, C=N), 1680 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 3.31 (s, 3H, NCH_3), 3.60 (m, 1H, CH), 3.88 (s, 3H, OCH_3), 7.02 (s, 1H, CH), 7.17, 7.65 (2d, 4H, *Ar*–H) ppm.

8-(1,3-Benzodioxol-5-yl)-3-isopropyl-5-methylthieno[3,2-e]-[1,2,4]triazolo[4,3-a]pyrimidin-4-one (**16b**, $C_{18}H_{16}N_4O_3S$)
From 0.74 g **15b** (2 mmol) and $FeCl_3$. Yield 0.47 g (64%) as brown powder; mp 175–177°C; IR (KBr): $\bar{\nu} = 1596$ (C=C, C=N), 1676 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 3.40 (m, 1H, CH), 3.60 (s, 3H, NCH_3), 6.20 (s, 1H, CH), 7.20 (m, 3H, *Ar*–H) ppm; $m/z = 368$ (M^+).

*General procedure for the synthesis of compounds **17a** and **17b***
A solution of 0.24 g **7b** (1 mmol) and an excess of isothiocyanate (2.5 mmol) in 10 cm^3 ethanol was boiled under reflux for 4 h. The product that separated after cooling was filtered off and recrystallized from ethanol.

2-(5-Isopropyl-3-methyl-4-oxo-3,4-dihydrothieno[2,3-d]-pyrimidin-2-yl)-N-phenylhydrazine carbothioamide
(**17a**, $C_{17}H_{19}N_5OS_2$)
From **7b** and 0.34 g phenyl isothiocyanate (2.5 mmol) as described before. Yield 0.27 g (73%) as colorless crystals; mp 264–266°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.25$ (d, 6H, $2CH_3$), 3.39 (s, 3H, NCH_3), 3.71 (m, 1H, CH), 7.15 (s, 1H, CH), 7.18, 7.33, 7.49 (m, 5H, *Ar*–H), 9.78 (s, 1H, NH), 14.06 (bd, 2H, 2NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.97$ ($2CH_3$), 27.20 (CH), 27.90 (N–CH_3), 114.66, 116.71, 141.09, 145.29 (thiophene), 123.48, 124.26, 128.29, 139.33 (*Ar*–C), 156 (C=N), 159.42 (C=O), 179.46 (C=S) ppm.

2-(5-Isopropyl-3-methyl-4-oxo-3,4-dihydrothieno[2,3-d]-pyrimidin-2-yl)-N-methylhydrazine carbothioamide
(**17b**, $C_{12}H_{17}N_5OS_2$)
From **7b** and 0.18 g, methyl isothiocyanate (2.5 mmol). Yield 0.22 g (70%) as colorless crystals; mp 201–203°C; IR (KBr): $\bar{\nu} = 1562$ (C=C, C=N), 1672 (C=O), 3137, 3325 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 2.89 (d, 3H, $NHCH_3$), 3.40 (s, 3H, NCH_3), 3.54 (m, 1H, CH), 6.75 (s, 1H, CH), 8.14, 9.27, 9.38 (3s, 3H, 3NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.74$ ($2CH_3$), 27.14 (CH), 28.19, 30.69 (2N–CH_3), 110.18, 113.76, 145.12, 151.46 (thiophene), 157.63 (C=N), 165.96 (C=O), 181.91 (C=S) ppm.

N-Allyl-2-(5-isopropyl-3-methyl-4-oxo-3,4-dihydrothieno-[2,3-d]pyrimidin-2-yl)hydrazine carbothioamide
(**17c**, $C_{14}H_{19}N_5OS_2$)
From **7b** and 0.25 g allyl isothiocyanate (2.5 mmol). Yield 0.24 g (71%) as white crystals; mp 168–170°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.40 (s, 3H, NCH_3), 3.54 (m, 1H, CH), 4.12 (d, 2H, CH_2), 5.03 (q, 2H, N–CH_2), 5.81 (m, 1H, CH), 6.75 (s, 1H, CH), 8.36, 9.31, 9.44 (3s, 3H, 3NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.74$ ($2CH_3$), 27.16 (CH), 28.19 (N–CH_3), 45.60 (CH_2), 110.17, 114.91, 145.10, 151.41 (thiophene), 113.72 (CH), 134.75 (N–CH_2), 157.68 (C=N), 166.03 (C=O), 181.66 (C=S) ppm.

3-Isopropyl-5-methyl-8-(methylamino)thieno[3,2-e][1,2,4]-triazolo[4,3-a]pyrimidin-4-one (**18**, $C_{12}H_{15}N_5OS$)
A mixture of 0.31 g **17b** (1 mmol) and 0.26 g mercuric oxide (1.2 mmol) in 25 cm^3 ethanol was heated under reflux for 2 h. The precipitate formed after cooling was filtered off, washed, and crystallized from ethanol as white crystals. Yield 0.22 g (70%); mp 192–194°C; IR (KBr): $\bar{\nu} = 1580$ (C=C, C=N), 1674 (C=O), 3255 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (d, 6H, $2CH_3$), 2.87 (d, 3H, $NHCH_3$), 3.46 (s, 3H, NCH_3), 3.72 (m, 1H, CH), 7.16 (s, 1H, CH) ppm; $m/z = 277$ (M^+).

N-(5-Isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)acetohydrazide (**19**, $C_{11}H_{14}N_4O_2S$)
A mixture of 2.24 g **7a** (10 mmol) in 15 cm^3 glacial acetic acid was boiled under reflux for 6 h. The reaction mixture was allowed to cool and poured into 100 cm^3 water. The separated solid was filtered off, dried, and crystallized from ethanol as pale brown powder. Yield 1.19 g (71%); mp 140–142°C; IR (KBr): $\bar{\nu} = 1603$ (C=C, C=N), 1661 (C=O), 3255 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.21$ (s, 6H, $2CH_3$), 1.91 (s, 3H, $COCH_3$), 3.49 (m, 1H, CH), 6.69 (s, 1H, CH), 8.73, 9.83, 11.27 (3s, 3H, 3NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 20.78$ (CH_3), 22.76 ($2CH_3$), 28.22 (CH), 109.24, 113.50, 145.13, 153.14 (thiophene), 158.41 (C=N), 168.09, 169.57 (2C=O) ppm.

2-[2-(Diphenylmethylene)hydrazino]-5-isopropyl-3-methyl-thieno[2,3-d]pyrimidin-4-one (**20**, $C_{23}H_{22}N_4OS$)
From 0.24 g **7b** (1 mmol) and 0.20 g benzophenone (1 mmol) as described for **10** as brown powder. Yield (0.32 g, 79%); mp 45–47°C; IR (KBr): $\bar{\nu} = 1652$ (C=C, C=N), 1674 (C=O), 3238 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.18$ (d, 6H, $2CH_3$), 3.29 (s, 3H, NCH_3), 3.56 (m, 1H, CH), 6.62 (s, 1H, CH), 7.58, 7.72 (m, 10H, 2*Ph*), 14.00 (bs, 1H, NH) ppm.

2-(3,5-Dimethyl-1-H-pyrazol-1-yl)-5-isopropyl-3-methyl-thieno[2,3-d]pyrimidin-4(3H)-one (**21**, $C_{14}H_{18}N_4OS$)
A mixture of 0.24 g **7b** (1 mmol) and 0.12 g pentane-2,4-dione (1.2 mmol) was heated under reflux for 6 h in 30 cm^3 absolute ethanol. The reaction mixture was allowed to cool. The solid product that separated was filtered off and recrystallized from ethanol as pale orange crystals. Yield 0.20 g

(66%); mp 115–117°C; IR (KBr): $\bar{\nu} = 1577$ (C=C, C=N), 1677 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 2.22, 2.34 (2d, 6H, $2CH_3$), 3.32 (s, 3H, NCH_3), 3.68 (m, 1H, CH), 6.16, 7.31 (2s, 2H, 2CH) ppm.

*General procedure for the synthesis of compounds **22a–22d***
A solution of 1 mmol **7a** or **7b** and an excess of the appropriate isocyanate (2.5 mmol) in 10 cm^3 ethanol was boiled under reflux for 4 h. The product that separated after cooling was filtered off and recrystallized from ethanol.

2-(5-Isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)-N-phenylhydrazine carboxamide (**22a**, $C_{16}H_{17}N_5O_2S$)
From **7a** and 0.30 g phenyl isocyanate (2.5 mmol). Yield 0.26 g (75%) as white crystals; mp 218–220°C; IR (KBr): $\bar{\nu} = 1548$ (C=C, C=N), 1623 (NHCONH), 1670 (C=O), 3321, 3386 (NH) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.50 (m, 1H, CH), 6.69 (s, 1H, CH), 6.96 (m, 1H, *Ar*–H), 7.75 (m, 2H, *Ar*–H), 7.46 (m, 2H, *Ar*–H), 8.15, 8.52, 8.77, 11.12 (4s, 4H, 4NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.77$ ($2CH_3$), 28.24 (CH), 109.42, 114.79, 145.18, 153.63 (thiophene), 118.41, 121.89, 128.58, 139.55 (*Ar*–C), 155.49 (C=N), 158.35, 168.06 (2C=O) ppm.

N-(4-Chlorophenyl)-2-(5-isopropyl-4-oxo-3,4-dihydrothieno-[2,3-d]pyrimidin-2-yl)hydrazine carboxamide
(**22b**, $C_{16}H_{16}ClN_5O_2S$)
From **7a** and 0.38 g 4-chlorophenyl isocyanate (2.5 mmol). Yield 0.28 g (76%) as white crystals; mp 200–202°C; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.50 (m, 1H, CH), 6.70 (s, 1H, CH), 7.32, 7.52 (2d, 4H, *Ar*–H), 8.24, 8.54, 8.94, 11.15 (4s, 4H, 4NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.76$ ($2CH_3$), 28.23 (CH), 109.41, 114.79, 145.15, 153.53 (thiophene), 119.97, 125.38, 128.37, 138.61 (*Ar*–C), 155.43 (C=N), 158.32, 167.99 (2C=O) ppm.

2-(5-Isopropyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)-N-(2-methylphenyl)hydrazine carboxamide
(**22c**, $C_{17}H_{19}N_5O_2S$)
From **7a** and 0.33 g *o*-tolyl isocyanate (2.5 mmol). Yield 0.27 g (76%) of white crystals; mp 166–168°C; IR (KBr): $\bar{\nu} = 1607$ (C=C, C=N), 1656 (C=O), 3237 (NH) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 2.22 (s, 3H, CH_3), 3.51 (m, 1H, CH), 6.70 (s, 1H, CH), 7.00 (m, 1H, *Ar*–H), 7.15 (m, 2H, *Ar*–H), 7.65 (d, 1H, *Ar*–H), 8.00, 8.39, 8.54, 11.12 (4s, 4H, 4NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 17.68$ (CH_3), 22.76 ($2CH_3$), 28.24 (CH), 109.38, 114.75, 145.16, 153.61 (thiophene), 121.92, 122.99, 123.19, 125.99, 130.08, 137.04 (*Ar*–C), 155.74 (C=N), 158.34, 168.06 (2C=O) ppm.

2-(5-Isopropyl-3-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)-N-phenylhydrazine carboxamide
(**22d**, $C_{17}H_{19}N_5O_2S$)
A solution of 0.24 g **7b** (1 mmol) and an excess of phenyl isocyanate (0.30 g, 2.5 mmol) in 10 cm^3 ethanol was boiled under reflux for 4 h. The separated product was filtered off and recrystallized from ethanol as colorless crystals. Yield 0.26 g (73%); mp 207–209°C; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.45 (s, 3H, NCH_3), 3.55 (m, 1H, CH), 6.72 (s, 1H, CH), 6.96 (m, 1H, *Ar*–H), 7.26 (m, 2H, *Ar*–H), 7.49 (m, 2H, *Ar*–H), 8.28, 8.81, 9.19 (3s, 3H, 3NH) ppm.

5-Isopropylthieno[2,3-d]pyrimidine-4(3H)-one
(**23**, $C_9H_{10}N_2OS$)
A solution of 0.69 g **22a** (2 mmol) and 25 cm^3 2 *M* sodium hydroxide was boiled for 1 h, then cooled and neutralized by addition of 2 *M* hydrochloric acid. The precipitate formed was collected, washed, and crystallized from ethanol as white powder. Yield 0.27 g (70%); mp 210–212°C; ^1H NMR (*DMSO*-d_6): $\delta = 1.27$ (s, 6H, $2CH_3$), 3.59 (m, 1H, CH), 7.18, 8.05 (2s, 2H, 2CH), 12.39 (bs, 1H, NH) ppm.

Ethyl-2-(5-isopropyl-3-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidin-2-yl)hydrazine carboxylate (**24**, $C_{13}H_{18}N_4O_3S$)
A mixture of 0.24 g **7b** (1 mmol) and 20 cm^3 ethyl chloroformate was heated under reflux for 4 h. The reaction mixture was allowed to cool. Evaporation of the solvent under reduced pressure and washing of the residue with *n*-hexane afforded a solid product, which was collected by filtration as yellow powder. Yield 0.20 g (65%); mp 143–145°C; IR (KBr): $\bar{\nu} = 1530$ (C=C, C=N), 1669 (NHCO), 1728 (C=O), 3258 (NH) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.19$ (t, 3H, CH_3), 1.21 (d, 6H, $2CH_3$), 3.53 (m, 1H, CH), 4.09 (q, 1H, CH), 6.73 (s, 1H, CH), 9.17, 9.25 (2s, 2H, 2NH) ppm; $m/z = 310$ (M^+).

*Synthesis of compounds **25a** and **26a***
A solution of 1.12 g **7a** or **7b** (5 mmol) in 10 cm^3 acetic acid was treated with a solution of 0.15 g sodium nitrite in 3 cm^3 H_2O at 5°C. The reaction mixture was allowed to stand at room temperature for 24 h with stirring. The solid product was filtered off and crystallized from ethanol to furnish colorless crystals. Yield 0.82 g (70%), mp 100–102°C.

2-Azido-5-isopropylthieno[2,3-d]pyrimidin-4(3H)-one
(**25a**, $C_9H_9N_5OS$) (*Major product*)
IR (KBr): $\bar{\nu} = 1573$ (C=C, C=N), 1663 (C=O), 2154 (N_3), 3445 (NH) ppm; ^1H NMR (*DMSO*-d_6): $\delta = 1.26$ (d, 6H, $2CH_3$), 3.61 (m, 1H, CH), 7.00 (s, 1H, CH), 12.60 (bs, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.67$ ($2CH_3$), 28.23 (CH), 111.20, 113.64, 115.81, 145.32 (thiophene), 147.45 (C=N), 165.00 (C=O) ppm.

6-Isopropyltetrazolo[1,5-a]thieno[3,2-e]pyrimidine-5(4H)-one (**26a**, $C_9H_9N_5OS$) (*Minor product*)
^1H NMR (*DMSO*-d_6): $\delta = 1.28$ (d, 6H, $2CH_3$), 4.15 (m, 1H, CH), 7.35 (s,1H,CH), 13.50 (bs, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.80$ ($2CH_3$), 27.71 (CH), 111.20, 113.64, 115.81, 145.32 (thiophene), 147.45 (C=N), 165.00 (C=O) ppm.

*Synthesis of compounds **25b** and **26b***
From 1.19 g **7b** (5 mmol) in 10 cm^3 acetic acid as described before to give colorless crystals. Yield 1.06 g (73%), mp 130–132°C.

2-Azido-5-isopropyl-3-methylthieno[2,3-d]pyrimidin-4-one (**25b**, $C_{10}H_{11}N_5OS$) (*Minor product*)
IR (KBr): $\bar{\nu} = 1604$ (C=C, C=N), 1676 (C=O), 2205 (N_3), 3120 (NH) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (d, 6H, $2CH_3$), 3.33 (s, 3H, NCH_3), 3.59 (m, 1H, CH), 7.05 (s, 1H, CH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 22.76$ (Me), 27.79 (CH), 30.04 (N–*Me*), 113.94, 116.02, 40.57, 147.29 (thiophene), 150.45 (C=N), 156.13 (C=O) ppm.

6-Isopropyl-4-methyletrtazolo[1,5-a]thieno[3,2-e]pyrimidin-5-one (**26b**, $C_{10}H_{11}N_5OS$) (*Major product*)
^1H NMR (*DMSO*-d_6): $\delta = 1.26$ (d, 6H, $2CH_3$), 3.61 (s, 3H, NCH_3), 3.66 (m, 1H, CH), 7.38 (s, 1H, CH) ppm.

2-Amino-5-isopropyl-3-methylthieno[2,3-d]pyrimidine-4-(3H)-one (**28**, $C_{10}H_{13}N_3OS$)
Zinc dust (0.08 g, 1.2 mmol) was added to a solution of 0.28 g **26b** (1 mmol) in 20 cm^3 acetic acid with stirring. The reaction mixture was heated at 80°C for 5 h and then left to cool at room temperature. The solid product that separated was filtered off and crystallized from ethanol to furnish pale brown crystals. Yield 0.08 g (35%); mp 180–182°C; IR (KBr): $\bar{\nu} = 1640$ (C=C, C=N), 1675 (C=O), 3132 (NH) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.18$ (d, 6H, $2CH_3$), 3.41 (s, 3H, NCH_3), 3.51 (m, 1H, CH), 6.54 (s, 1H, CH), 7.03 (s, 2H, NH_2) ppm.

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