# Formation of novel pyrido[3',2':4,5]thieno [2,3-*e*][1,2,4]triazolo[4,3-*c*] pyrimidines and their acyclic *C*-nucleosides analogues: synthesis of 3-(Alditol-1-yl)pyridothienotriazolopyrimidines

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A series of the hydrazones were prepared by the reaction of 4-hydrazino-7,9-dimethylpyrido[3',2':4,5]thieno [2,3-*d*]pyrimidine (**1**) with monosaccharides, and their acetylation was studied. The oxidative cyclisation of the hydrazones **3a–c** gave 3-(Alditol-1-yl)-pyridothienotriazolopyrimidenes **5a–c**, whose acetylation was carried out. Also, oxidative cyclisation of arylidenes **7a,b** gave the pyridothienotriazolopyrimidines **8a,b**.

**Keywords:** pyridothienotriazolopyrimidines, C-nucleosides, fused 1,2,4-triazoles

Fused heterocycles, containing the 1,2,4-triazole nucleus, have been the subject of many chemical and biological studies.[1-6] Considerable attention has been drawn to the synthesis of condensed heterocyclic system derived from 1,2,4-triazoles and pyridothienopyrimidines.[7-11] In continuation of our ongoing search for new heterocycles containing the pyridothienopyrimidine moiety,[12-15] of biological interest, we report here the synthesis of new pyridothienotriazolopyrimidines linked to alditolyl residues which it could be of potential biological properties. The respective *C*-nucleoside analogues are target molecules in this study owing to their great value from the biological point of view.[16]

Since the formation of aldose heteroarylhydrazines has been previously reported in the literature.[17] Aldehyde hydrazones, with a hydrazono group attached at the $\alpha$-position with respect to the ring nitrogen atom, can be oxidatively cyclised into the corresponding triazolo derivatives.[18-21] We decided to apply this synthesis also to the preparation of new 3-(alditol-1-yl) pyridothienotriazolopyrimidines. For this purpose D-galactose (**2a**), D-mannose (**2b**), D-arabinose (**2c**) and D-xylose (**2d**), were chosen as representative aldoses, and 4-hydrazino-7,9-dimethylpyridothienopyrimidine **1** was chosen as heteroarylhydrazine. The required starting material, **1** was prepared by adopting the earlier reported procedure from 7,9-dimethylpyridothienopyrimidinone by sequential chlorination with phosphorus oxychloride, then reaction with hydrazine hydrate.[22] Acid-catalysed reaction of hydrazino compound **1** with aldoses **2a–d** in refluxing ethanol resulted in the formation of the corresponding hydrazones **3a–d**. Acetylation of **3a–d** with acetic anhydride in pyridine gave, respectively, the acetyl derivatives **4a–d**, whose combustion analysis indicated that peracetylation had taken place on both the alditolyl residue and on the NH group. Their IR spectra showed absorptions indicating the presence of OAc and NAc groups (Table 1). $^1$H NMR spectra of **4a–d** confirmed the presence of an NAc group at $\delta$ = 2.42–2.43, in addition to the five OAc groups that appeared as five singlets in **4a,b** and four OAc groups that appeared as four singlets in **4c,d**. The doublet at low field

**Table 1** Experimental and infrared data of compounds **3–6**

| Compd | Mp/°C Solvent | Yield/% | Mol. Formula Mol. Wt | Analysis Calcd / Found C, | H, | N % | IR (KBr) |
|---|---|---|---|---|---|---|---|
| **3a** | 208–210<br>DMF | 70 | $C_{17}H_{21}N_5O_5S$<br>407.45 | 50.11,<br>49.92, | 5.19,<br>5.16, | 17.19<br>17.11 | 3323 (OH), 3210 (NH), 1567 (C=N). |
| **3b** | 227–229<br>DMF | 84 | $C_{17}H_{21}N_5O_5S$<br>407.45 | 50.11,<br>50.42, | 5.19,<br>5.13, | 17.19<br>16.82 | 3323 (OH), 3198 (NH), 1567 (C=N). |
| **3c** | 216–218<br>DMF | 78 | $C_{16}H_{19}N_5O_4S$<br>377.42 | 50.92,<br>50.61, | 5.07,<br>4.87, | 18.56<br>18.45 | 3331 (OH), 3205 (NH), 1569 (C=N). |
| **3d** | 175–177<br>DMF | 73 | $C_{16}H_{19}N_5O_4S$<br>377.42 | 50.92,<br>50.55, | 5.07,<br>5.35, | 18.56<br>18.77 | 3331 (OH), 3222 (NH), 1565 (C=N). |
| **4a** | 196–198<br>EtOH | 85 | $C_{29}H_{33}N_5O_{11}S$<br>659.67 | 52.80,<br>52.56, | 5.04,<br>4.84, | 10.62<br>10.21 | 1755 (O*CO*), 1693 (N*CO*) |
| **4b** | 179–181<br>EtOH | 88 | $C_{29}H_{33}N_5O_{11}S$<br>659.67 | 52.80,<br>52.50, | 5.04,<br>4.94, | 10.62<br>11.00 | 1749 (O*CO*), 1698 (N*CO*) |
| **4c** | 186–188<br>EtOH | 72 | $C_{26}H_{29}N_5O_9S$<br>587.60 | 53.14,<br>52.86, | 4.97,<br>5.22, | 11.92<br>12.24 | 1746 (O*CO*), 1697 (N*CO*) |
| **4d** | 165–167<br>EtOH | 48 | $C_{26}H_{29}N_5O_9S$<br>587.60 | 53.14,<br>53.36, | 4.97,<br>5.32, | 11.92<br>11.64 | 1755 (O*CO*), 1702 (N*CO*) |
| **5a** | 196–198<br>DMF | 50 | $C_{17}H_{19}N_5O_5S$<br>405.43 | 50.36,<br>50.22, | 4.72,<br>4.42, | 17.27<br>17.43 | 3318 (OH), 1625 (C=N). |
| **5b** | DMF | 36 | $C_{17}H_{19}N_5O_5S$<br>405.43 | 50.36,<br>50.66, | 4.72,<br>4.43, | 17.27<br>16.95 | 3261 (OH), 1627 (C=N). |
| **5c** | 229–232 | 38 | $C_{16}H_{17}N_5O_4S$<br>375.40 | 51.19,<br>50.96, | 4.56,<br>4.18, | 18.66<br>18.67 | 3325 (OH), 1621 (C=N). |
| **6a** | 173–175<br>EtOH | 75 | $C_{27}H_{29}N_5O_{10}S$<br>615.61 | 52.68,<br>52.43, | 4.75,<br>4.45, | 11.38<br>11.20 | 1752 (O*CO*), 1623 (C=N) |
| **6b** | 196–198<br>EtOH | 67 | $C_{27}H_{29}N_5O_{10}S$<br>615.61 | 52.68,<br>52.77, | 4.75,<br>4.33, | 11.38<br>11.25 | 1751 (O*CO*), 1624 (C=N) |
| **6c** | 192–194<br>EtOH | 75 | $C_{24}H_{25}N_5O_8S$<br>543.55 | 53.03,<br>53.25, | 4.64,<br>4.45, | 12.88<br>13.10 | 1752 (O*CO*), 1620 (C=N) |

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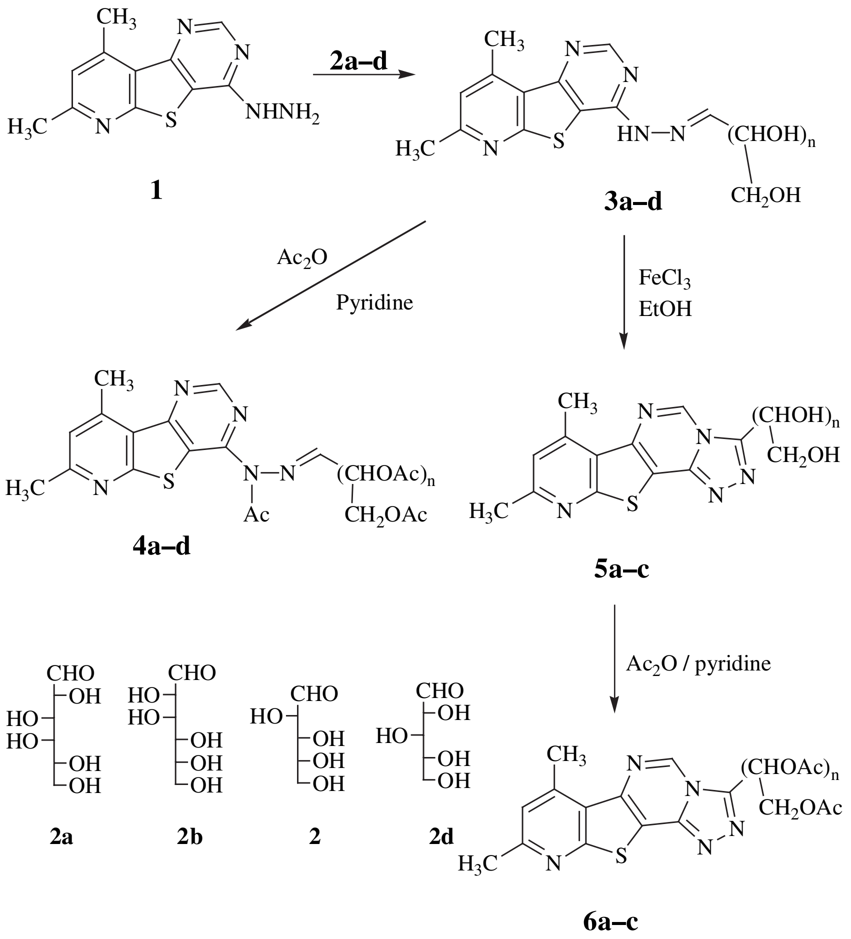
**Table 2** $^1H$ NMR spectral data for compounds **3** and **4** in DMSO

| H Assigment | Chemical shift (δ) / Coupling constant (Hz) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **3a** | **3b** | **3c** | **3d** | **4a** | **4b** | **4c** | **4d** |
| Alditolyl protons | | | | | | | | |
| H-1 | 7.61 (d) | 7.52 (d) | 7.58 (d) | 7.54 (d) | 6.78 (d) | 7.41 (d) | 6.84 (d) | 6.84 (d) |
| $J_{1,2}$ | 5.7 | 6.6 | 6.0 | 6.3 | 2.7 | 4.8 | 3.0 | 4.2 |
| H-2 | 4.97 | 5.23 (d) | 5.08 (d) | 5.17 (d) | 5.49 (t) | 5.48 (m) | 5.58 (t) | 5.54 (t) |
| $J_{2,3}$ | 5.7 | 5.1 | 6.0 | 3.9 | 2.4 | | 3.3 | 4.4 |
| H-3 | 4.59 (d) | 4.30 (m) | 4.46 (m) | 4.37 (m) | 5.33(dd) | 5.48 (m) | 5.41(dd) | 5.41 (t) |
| $J_{3,4}$ | 6.3 | | | | 1.7, 5.3 | | 2.9, 8.0 | 5.1 |
| H-4 | 4.49 (m) | 4.30 (m) | 3.66 (m) | 4.37 (m) | 5.33 (m) | 5.48 (m) | 5.21(m) | 5.23 (q) |
| $J_{4,5}$ | | | | | | | | 5.4 |
| H-5 | 4.49 (m) | 4.30 (m) | 3.66 (m) | 4.37 (m) | 5.18 (m) | 5.16(m) | 4.19(dd) | 4.16 (dd) |
| $J_{5,5'}$ | | | | | | | 5.6,12.5 | 6.5, 12.3 |
| H-5' | | | 3.66 (m) | 4.37 (m) | | | 4.15(dd) | 3.98 (dd) |
| $J_{4,5'}$ | | | | | | | 2.6,12.5 | 4.2, 11.7 |
| H-6 | 4.28 (d) | 4.30 (m) | | | 4.13(dd) | 4.20(dd) | | |
| $J_{5,6'}$ | 6.0 | | | | 4.1, 11.9 | 2.9,12.5 | | |
| H-6' | 4.20 (d) | 4.30 (m) | | | 3.91(dd) | 4.11(dd) | | |
| $J_{6,6''}$ | 6.6 | | | | 7.2, 11.7 | 5.3,12.5 | | |
| NAc | | | | | 2.42 (s) | 2.42 (s) | 2.43 (s) | 2.43 (s) |
| OAc | | | | | 2.09 (s) | 2.12 (s) | 2.07 (s) | 2.08 (s) |
| OAc | | | | | 2.05 (s) | 2.09 (s) | 2.04 (s) | 2.03 (s) |
| OAc | | | | | 1.98 (s) | 2.01 (s) | 1.98 (s) | 2.02 (s) |
| OAc | | | | | 1.95 (s) | 2.01 (s) | 1.95 (s) | 1.96 (s) |
| OAc | | | | | 1.93 (s) | 1.96 (s) | | |
| OH's | 3.61 (m) | 3.61(m) | 3.62(m) | 3.62 (m) | | | | |
| NH | 11.72(bs) | 11.74(bs) | 11.74(bs) | 11.73(bs) | | | | |
| Protons on the heterocyclic ring | | | | | | | | |
| H-2 | 8.62 (s) | 8.64 (s) | 8.65 (s) | 8.63 (s) | 9.34 (s) | 8.69 (s) | 9.40 (s) | 9.43 (s) |
| H-8 | 7.20 (s) | 7.24 (s) | 7.25 (s) | 7.22 (s) | 7.45 (s) | 7.27 (S) | 7.45 (s) | 7.45 (s) |
| $CH_3$ | 2.91 (s) | 2.93 (s) | 2.94 (s) | 2.94 (s) | 3.00 (s) | 2.93 (s) | 3.01 (s) | 3.00 (s) |
| $CH_3$ | 2.58 (s) | 2.60 (s) | 2.60 (s) | 2.59 (s) | 2.64 (s) | 2.60 (s) | 2.65 (s) | 2.65 (s) |



**Scheme 1**

**Table 3** $^1$H NMR spectral data of compounds **5c** and **6a–c**

| H | | | | |
|---|---|---|---|---|
| Assigment | Chemical shift (δ) / Coupling constant (Hz) | | | |
| | **5c** | **6a** | **6b** | **6c** |
| Alditolyl protons | | | | |
| H-1 | 5.21 | 6.16 (d) | 5.97 (d) | 6.31 (d) |
| $J_{1,2}$ | | 2.7 | 8.4 | 3.6 |
| H-2 | | 5.53 (m) | 5.63 (m) | 5.71 (dd) |
| $J_{2,3}$ | | | | 3.3, 7.8 |
| H-3 | 4.64 | 5.53 (m) | 5.63 (m) | 5.25 (m) |
| H-4 | 4.46 | 5.28 (m) | 5.10 (m) | 4.31 (dd) |
| $J_{3,4}$ | | | | 2.7, 12.00 |
| H-4' | 4.29 | | | 4.21 (dd) |
| $J_{4,4'}$ | | | | 5.3, 12.5 |
| H-5 | | 4.22 (dd) | 4.22 (dd) | |
| $J_{5,5'}$ | | 4.8, 12 | 3, 12.3 | |
| H-5' | | 3.98 (m) | 4.11 (dd) | |
| $J_{4,5'}$ | | | 5.4, 12.3 | |
| OAc | | 2.13 (s) | 2.15 (s) | 2.20 (s) |
| OAc | | 1.99 (s) | 2.12 (s) | 2.06 (s) |
| OAc | | 1.98 (s) | 1.99 (s) | 2.02 (s) |
| OAc | | 1.94 (s) | 1.98 (s) | 1.99 (s) |
| OAc | | 1.91 (s) | 1.91 (s) | |
| OH's | 3.9,3.64, 3.48(bs) | | | |
| Protons on the heterocyclic ring | | | | |
| H-5 | 9.78 (s) | 9.88 (s) | 9.87 (s) | 9.85 (s) |
| H-8 | 7.31 (s) | 7.38 (s) | 7.35 (s) | 7.30 (s) |
| $CH_3$ | 2.93 (s) | 2.98 (s) | 2.95 (s) | 2.90 (s) |
| $CH_3$ | 2.60 (s) | 2.63 (s) | 2.62 (s) | 2.60 (s) |

(δ = 6.78–7.41) was assigned to H-1, followed by the rest of the alditol-1-yl side chain at higher field (Table 2). The $^{13}$C NMR spectra (Table 4) of **4a–d** have been studied. The spectra showed resonances in the high field region corresponding to the methyl carbons, followed by the sugar carbons and then the heterocyclic ring carbons followed by the carbonyl carbons in the acetyl groups. Cyclisation of aldose hydrazones **3a–c** into the corresponding triazoles **5a–c** was achieved by the action of ethanolic iron (III) chloride. Acetylation of **5a–c** gave the per-*O*-acetyl derivatives **6a–c**. The IR spectra of **6a–c** showed the presence of only one absorption in the carbonyl frequency region (OAc). The $^1$H NMR spectra of **6a–c** didn't show signals that could be attributed to the *N*-acetyl group, but the rest of the spectrum has almost the same pattern as that of the **4a–c**. (Table 3). $^{13}$C NMR spectrum of **6c** showed six methyl carbons that appeared as six signals at δ = 19.00–23.40 region, followed by four signals at δ = 61.35–69.72 region corresponding to sagur carbons and then ten signals at δ = 116.90–163.08 region corresponding to 10 carbons in the fused heterocyclic rings, followed by four carbonyl carbons at δ = 169.08–169.93 region (Table 4)

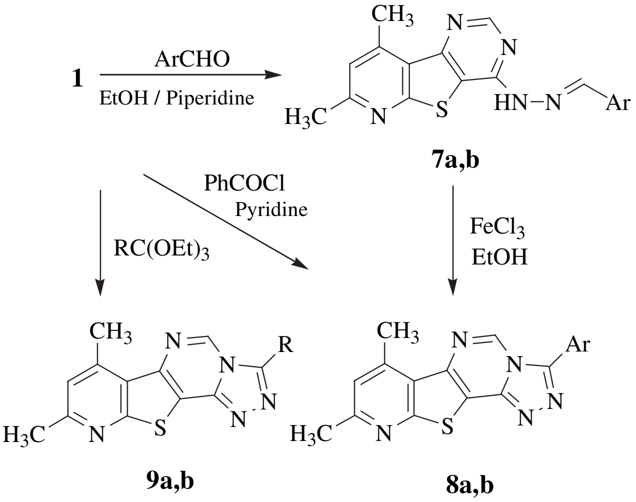
A model study for this cyclisation has also been done on the arylidene derivatives **7a,b**, which were prepared by condensation of **1** with aromatic aldehydes. Oxidative cyclisation of **7a,b** with iron (III) chloride gave the triazolo derivatives **8a,b**. An independent synthesis of **8a** by cyclocondensation of **1** with benzoyl chloride in dry pyridine, which was identical in all physical and spectroscopic aspects with the compound obtained by oxidative cyclisation of **7a**. Also, cyclocondensation of **1** with triethyl orthoformate or triethyl orthoacetate afforded the triazoles **9a,b** in good yield (Scheme 2). The structural assignments of the new compounds were made on the basis of spectral and analytical data.

## Experimental

Melting points were determined on a Buchi melting point and are uncorrected. $^1$H NMR spectra were recorded on a Varian Gemini-2000 (300MHz) and registered in DMSO-d6, and chemical shifts are expressed in parts per million (δ) relative to internal $Me_4Si$. IR spectra were recorded on a Nicolet FT-IR spectrophotometer. Mass spectra were measured on a Kratos 50 tc spectrometers. Microanalysis performed in microanalysis lab at Cairo University. Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard

**Table 4** $^{13}$C NMR spectral data of some compounds in DMSO

| Compd No | Carbons of the sugar part | Carbons of the heterocyclic ring | Miscellaneous carbons | | | |
|---|---|---|---|---|---|---|
| | | | Me | OCO$CH_3$ | NCO-$CH_3$ | X$CO$ |
| **3b** | 63.73, 69.41, 70.69, 70.79, 71.17, 110.76 | 122.09, 122.54, 146.26, 148.70, 153.93, 156.14, 156.48, 159.71, 164.10 | 19.38, 24.09 | | | |
| **3c** | 63.33, 70.38, 70.89, 73.52, 110.69 | 122.12, 122.56, 146.28, 148.87, 154.00, 156.18, 156.51, 159.73, 164.02 | 19.36, 24.04 | | | |
| **4a** | 61.72, 67.12, 67.18, 67.44, 69.63, 128.26 | 122.22, 123.17, 143.28, 147.78, 152.03, 155.35, 160.01, 162.19, 162.36 | 19.20, 24.16 | 20.26, 20.32, 20.32, 20.40, 20.40, | 21.44 | 168.96, 169.21, 169.30, 169.45, 169.84, 170.85. |
| **4b** | 61.37, 67.04, 67.59, 68.68, 69.85, 128.33 | 122.26, 122.44, 139.32, 146.46, 153.85, 156.09, 156.50, 159.96, 162.43, | 19.35, 24.02 | 20.33, 20.40, 20.40, 20.49, 20.67, | 21.34 | 169.01, 169.30, 169.39, 169.46, 169.92, 170.89. |
| **4c** | 61.38, 67.70, 68.55, 69.83, 128.26 | 122.28, 123.17, 143.45, 147.78, 152.01, 155.37, 160.09, 162.17, 162.36 | 19.20, 24.17 | 20.30, 20.34, 20.39, 20.39, | 21.45 | 169.13, 169.13, 169.18, 169.88, 170.89. |
| **4d** | 61.53, 68.46, 69.14, 70.76, 128.26 | 122.29, 123.15, 142.68, 147.75, 151.87, 155.35, 160.17, 160.16, 162.40 | 19.20, 24.17 | 20.32, 20.32, 20.42, 20.45 | 21.40 | 169.15, 169.33, 169.34, 169.83, 170.92 |
| **6c** | 61.35, 66.93, 67.97, 69.72 | 116.90, 122.99, 123.03, 138.86, 145.08, 145.71, 148.08, 159.41, 160.35, 163.08 | 19.00, 23.84 | 20.26, 20.38, 20.40, 20.43 | | 169.08, 169.27, 169.39, 169.93 |



**9a**, R = H
**9b**, R = $CH_3$

**7a**, **8a**, Ar = $C_6H_5$
**7b**, **8b**, Ar = *p* F-$C_6H_5$

**Scheme 2**

literature procedures. All reactions were monitored by TLC, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using UV light (254 and 360 nm) for detection.

*Sugar (7,9-dimethylpyrido[3',2':4,5]thieno[3,2-d]pyrimidin-4-yl) hydrazones **3a–d:** general procedure*

To a mixture of **1** (0.6 g, 2.5 mmol) and the appropriate aldose **2a–d** (2.5 mmol) in ethanol (15 ml), a catalytic amount of glacial acetic acid (0.1 ml) was added. The reaction mixture was heated under reflux on a water bath for 45 min. After cooling at room temperature, the precipitated solid was collected by filtration and recrystallised from DMF to give the products **3a–d** (Tables 1 and 2).

*Per-O-acetyl-sugar{1-acetyl-1-(7,9-dimethylpyrido[3',2':4,5]thieno [3,2-d]pyrimidin-4-yl)}hydrazones* **4a–d:** *general procedure*

To a cold suspension of **3a–d** (1.23 mmol) in dry pyridine (10 ml), acetic anhydride (5 ml) was added dropwise, and the reaction mixture was stirred at room temperature for 48 h. The reaction mixture was poured onto crushed ice, and the product was collected by filtration, washed repeatedly with water and recrystallised from EtOH to give the products **4a–d** (Tables 1 and 2).

*3-(Alditol-1-yl)-7,9-dimethylpyrido[3',2':4,5]thieno[2,3-e][1,2,4] triazolo[4,3-c]pyrimidine* **5a–c**: *general procedure*

A solution of iron (III) chloride in ethanol (2M) (1.6 g, 10 ml) was added dropwise to a boiling suspension of compound **3a–c** (1 mmol) in ethanol (10 ml). Heating was continued for an additional 10 min, and the mixture was then kept at room temperature for 48 h. The resulting solid product was filtered, washed repeatedly with water, dried and recrystallised from DMF (Tables 1 and 3).

*3-(Polyacetoxyalkyl)pyrido[3',2':4,5]thieno[2,3-e][1,2,4]triazolo [4,3-c]pyrimidines* **6a–c**: *general procedure*

To a cold suspension of **5a–c** (1 mmol) in dry pyridine (10 ml), acetic anhydride (5 ml) was added dropwise and the mixture was stirred at room temperature for 48 h. The reaction mixture was poured onto ice-cold water and the separated solid product was collected by filteration, washed with water (3 times), dried and recrystallised from ethanol (Tables 1 and 3).

*4-(Arylidenehydrazino)pyrido[3',2':4,5]thieno[3,2-d]pyrimidines* **7a,b**: *general procedure*

To a mixture **1** (0.6 g, 2.5 mmol) and the appropriate aromatic aldehydes (2.5 mmol) in absolute ethanol (10 ml), a catalytic amount of piperidine was added. The reaction mixture was refluxed for 3 h. After concentration and cooling at room temperature, the precipitated product was filtered off, dried and recrystallised from methanol.

*7,9-dimethyl-4-(benzyllidenehydrazino)pyrido[3',2':4,5]thieno[ 3,2-d]pyrimidine* (**7a**): Colourless prisms, (0.7 g, 88%), m.p. 317–320 °C; IR: $\nu_{max}$ 3400 (NH), 1620 (C=N) $cm^{-1}$.$^1H$ NMR (DMSO): δ = 2.60 (s, 3H, $CH_3$), 2.95 (s, 3H, $CH_3$), 7.24 (s, 1H, H-8), 7.43–7.85 (m, 5H, Ar–H), 8.22 (s, 1H, N=CH), 8.69 (s, 1H, H-2), 12.12 (bs, 1H, NH). Found: C 64.70 H 4.33 N 20.90 Calcd. for $C_{18}H_{15}N_5S$(333.41): C 64.84 H 4.53 N 21.01

*7,9-Dimethyl-4-(4-florobenzyllidenehydrazino)pyrido[3',2':4,5] thieno[3,2-d]pyrimidine* (**7b**): Colourless prisms, (0.8 g, 88%), m.p. 310–312 °C; IR: $\nu_{max}$ 3380 (NH), 1620 (C=N) $cm^{-1}$.$^1H$ NMR (DMSO): δ = 2.58 (s, 3H, $CH_3$), 2.83 (s, 3H, $CH_3$), 7.21 (s, 1H, H-8), 7.34–7.40 (m, 2H, Ar–H), 7.83–7.88 (m, 2H, Ar–H), 8.18 (s, 1H, N=CH), 8.67 (s, 1H, H-2), 12.09 (bs, 1H, NH). Found: C 61.75 H 3.96 N 19.58. Calcd.for $C_{18}H_{14}FN_5S$ (351.40): C 61.52 H 4.02 N 19.93.

*3-Aryl-7,9-dimethylpyrido[3',2':5,4]thieno[2,3-e][1,2,4]triazolo [4,3-c]pyrimidines* **8a,b**: *general procedure*

A solution of iron (III) chloride in ethanol (2 M)(1.6 g in 5 ml EtOH) was added in dropwise to a boiling solution of **7a,b** (1.2 mmol) in absolute ethanol (30 ml), then the reaction mixture was boiled for 10 min. After cooling at room temperature, the resulting solid product was collected by filtration, washed with water, died and recrystallised from acetic acid.

*7,9-Dimethyl-3-phenylpyrido[3',2':5,4]thieno[2,3-e][1,2,4] triazolo[4,3-c]pyrimidine* (**8a**)**:** Colourless prisms, (0.3 g, 63%), m.p. 280–282 °C. IR: $\nu_{max}$ 3100 (arom. CH), 2950 (aliph. CH), 1620 (C=N) $cm^{-1}$. $^1H$ NMR (DMSO): δ = 2.49 (s, 3H, $CH_3$), 2.96 (s, 3H, $CH_3$), 7.34 (s, 1H, H-8), 7.55–8.24 (m, 5H, Ar–H), 9.84 (s, 1H, H-2). Found: C 65.36 H 3.99 N 21.18. Calcd. for $C_{18}H_{13}N_5S$ (331.40): C 65.24 H 3.95 N 21.13;

*7,9-Dimethyl-3-(4-florophenyl)pyrido[3',2':5,4]thieno[2,3-e][1,2,4] triazolo[4,3-c]pyrimidine* (**8b**): Colourless prisms, (0.3 g, 75%), m.p. 335–337 °C. IR: $\nu_{max}$ 3000 (arom. CH), 2950 (aliph. CH), 1620 (C=N) $cm^{-1}$. $^{-1}H$ NMR (DMSO): δ = 2.66 (s, 3H, $CH_3$), 2.89 (s, 3H, $CH_3$), 7.41 (s, 1H, H-8), 7.68–8.35 (m, 4H, Ar–H), 9.90 (s, 1H, H-2). Found: C 61.90 H 3.52 N 20.08 Calcd. for $C_{18}H_{12}FN_5S$ (349.39): C 61.88 H 3.46 N 20.04

*Synthesis of* **8a** *from 7,9-dimethyl-4-hydrazino[3',2':4,5]thieno [2,3-d]pyrimidine* **1**

A mixture of **1** (0.49 g, 2 mmol) and benzoyl chloride (0.54g, 4 mmol) was heated under reflux in anhydrous pyridine (10 ml) for 8 h. After cooling at room temperature and dilution with ice-cold water, the resulting solid product was filtered off, dried and recrystallised from AcOH to give **8a** in 75%.

*Pyrido[3',2':4,5]thieno[2,3-e][1,2,4]triazolo[4,3-c]pyrimidines* **9a,b**: *general procedure*

A mixture of **1** (0.6g, 2.5 mmol) and triethyl orthoformate or triethyl orthoacetate was heated under reflux for 5 h. After concentration and cooling at room temperature, the reaction mixture was poured onto ice-cold water. The resulting solid product was collected by filtration, washed with methanol, dried and recrystallised from acetic acid.

*7,9-Dimethylpyrido[3',2':4,5]thieno[2,3-e][1,2,4]triazolo[4,3-c] pyrimidine* (**9a**):

Colourless prisms, (0.4 g, 67%), m.p. 282–284 °C. IR: $\nu_{max}$ 3100 (arom. CH), 2940 (aliph. CH), 1620 (C=N) $cm^{-1}$.-1H NMR (DMSO): δ = 2.63 (s, 3H, $CH_3$), 2.98 (s, 3H, $CH_3$), 7.36 (s, 1H, H-8), 8.77 (s, 1H, H-3), 9.88 (s, 1H, H-2). Found: C 56.22, H 3.65, N 27.25 Calcd.for $C_{12}H_9N_5S$ (255.30): C 56.45, H 3.55, N 27.43

*3,7,9-Trimethylpyrido[3',2':4,5]thieno[2,3-e][1,2,4]triazolo[4,3-c] pyrimidine* (**9b**)**:**

Colourless prisms, (0.2 g, 67%), m.p. 262–264 °C; IR: $\nu_{max}$ 3050 (arom. CH), 2980 (aliph. CH), 1610 (C=N) $cm^{-1}$.-$^1H$ NMR (DMSO): δ = 2.50 (s, 3H, $CH_3$), 2.57 (s, 3H, $CH_3$), 2.93 (s, 3H, $CH_3$), 7.30 (s, 1H, H-8), 9.70 (s, 1H, H-2). -Ms (EI, 70 eV): *m/z* (%) = 269 (100) [M+], 200 (5), 97 (15). Found: C 58.01, H 4.16, N 26.03. Calcd. for $C_{13}H_{11}N_5S$ (269.33): C 57.97, H 4.12, N 26.00.

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