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A FACILE ONE-POT SYNTHESIS OF SULFUR-LINKED THIENO[1,2,4]-TRIAZOLO[4,3-*c*]PYRIMIDINE DERIVATIVES CONTAINING PHENYLPYRAZOLE OR THIENOPYRIMIDINYLPYRAZOLE MOIETY

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Abstract – A facile synthesis of sulfur-linked thieno[1,2,4]triazolo[4,3-*c*]pyrimidine derivatives containing phenylpyrazole or thienopyrimidinylpyrazole moiety via a one-pot reaction of thieno[1,2,4]triazolo[4,3-*c*]pyrimidine-3(2*H*)-thiones, 3-chloropentane-2,4-dione and various hydrazines in the presence of potassium hydroxide in ethanol has been achieved.

Thienotriazolopyrimidine derivatives have attracted much attention and are of great interest as potential therapeutic agents. For instance, thienotriazolopyrimidine **1** as shown in Figure 1 and its analog have been recently explored for inhibitor of Shiga toxin trafficking and A₁/A_{2A} or A_{2A}/A₃ adenosine receptor antagonists, respectively.^{1,2} We have previously designed and synthesized thienotriazolopyrimidine derivatives **2** with promising biological activity using iodobenzene diacetate.³ Moreover, sulfur-containing 1,2,4-triazoles (3-thio-1,2,4-triazoles) were also reported to possess an impressive array of biological activities such as antibacterial, antifungal, analgesic, somatostatin sst₂/sst₅ agonist and carbonic anhydrase inhibitor.⁴⁻⁷ Particularly, sulfur-linked heterocyclic compounds containing triazolopyrimidine or pyrazole such as **3** and **4** were investigated for antifungal agent and dopamine D₃ receptor antagonist, respectively.^{8,9} We also have recently reported the synthesis of diheterocyclic compound **5** and its analogs.¹⁰ In the other hand, many pyrazole derivatives are reported to possess a broad spectrum of biological activities, such as antifungal, anti-inflammatory, A₃ adenosine receptor antagonist, etc.¹¹⁻¹³

Therefore, we devised the introduction of 1*H*-pyrazole moiety to the thieno[1,2,4]triazolo[4,3-*c*]pyrimidine ring by sulfur to produce novel di- and triheterocyclic systems using the concept of molecular

hybridization.¹⁴ As a continuation of our synthetic works on heterocyclic compounds related to thienopyrimidines and thienopyridines with biological interest,¹⁵ we wish to report herein the facile one-pot synthesis of new sulfur-linked heterocyclic compounds **7a-i** and **9a-i** having thieno[1,2,4]triazolo[4,3-*c*]pyrimidine and pyrazole ring, which are structurally related to **4** and **5** in the hope of obtaining compounds of diverse biological activities.

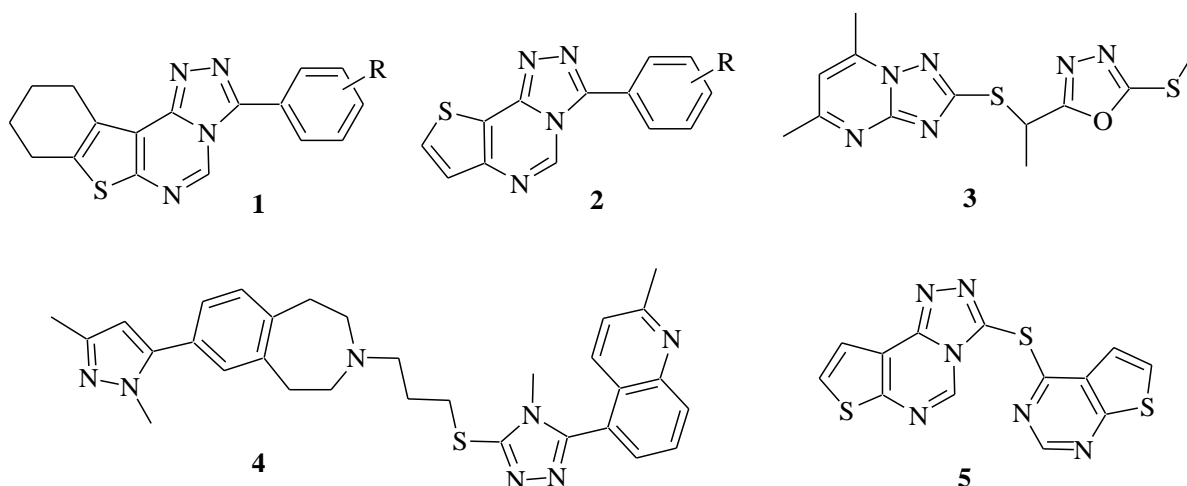
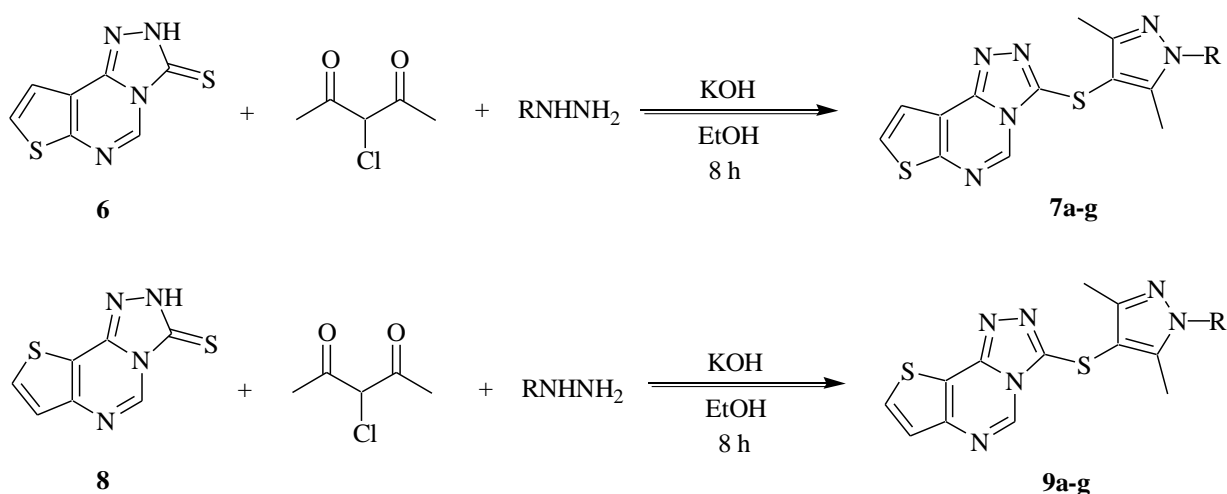


Figure 1. Compounds 1-5

The initial one-pot reactions were performed by adding 3-chloropentane-2,4-dione and a phenylhydrazine to thieno[1,2,4]triazolo[4,3-*c*]pyrimidine-3(2*H*)-thione **6** or **8**¹⁰ in the presence of sodium acetate in refluxing methanol for 24 h. After evaporation of the solvent, the residue was extracted with ethyl acetate, and the solution was concentrated to afford crude product with side products. The pure solid products were obtained in moderate yield after recrystallization in ethanol.



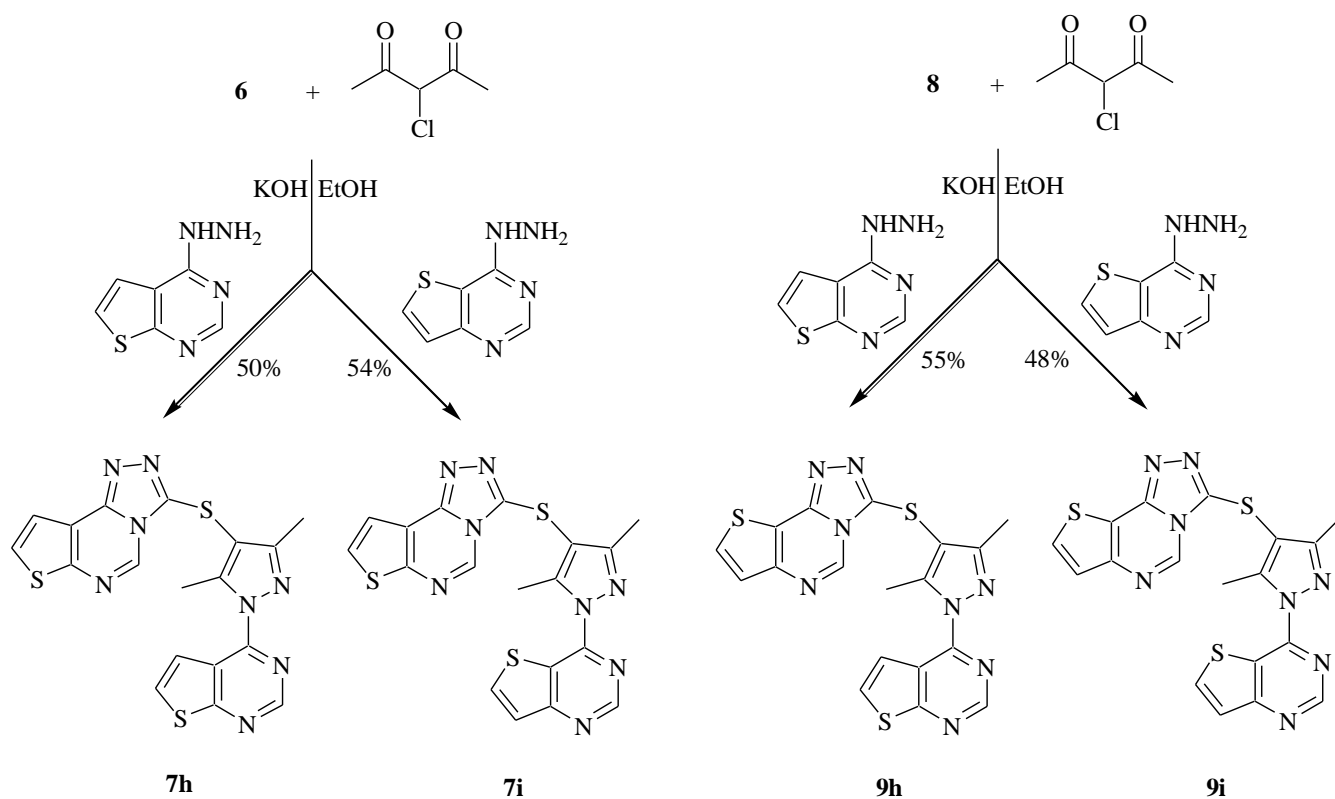
Scheme 1. Synthesis of diheterocyclic compounds in one-pot reaction

To explore the optimal condition of this one-pot reaction, various reaction conditions were investigated, including solvent (THF, DMF, EtOH, CH₃CN), base (CH₃CO₂Na, KOH, K₂CO₃, Et₃N) and temperature variations (rt and reflux). It was observed that the reaction using potassium hydroxide (2 eq) as base in refluxing ethanol for 8 h gave the best result (Scheme 1).

Table 1. Diheterocyclic compounds **7a-g** and **9a-g**

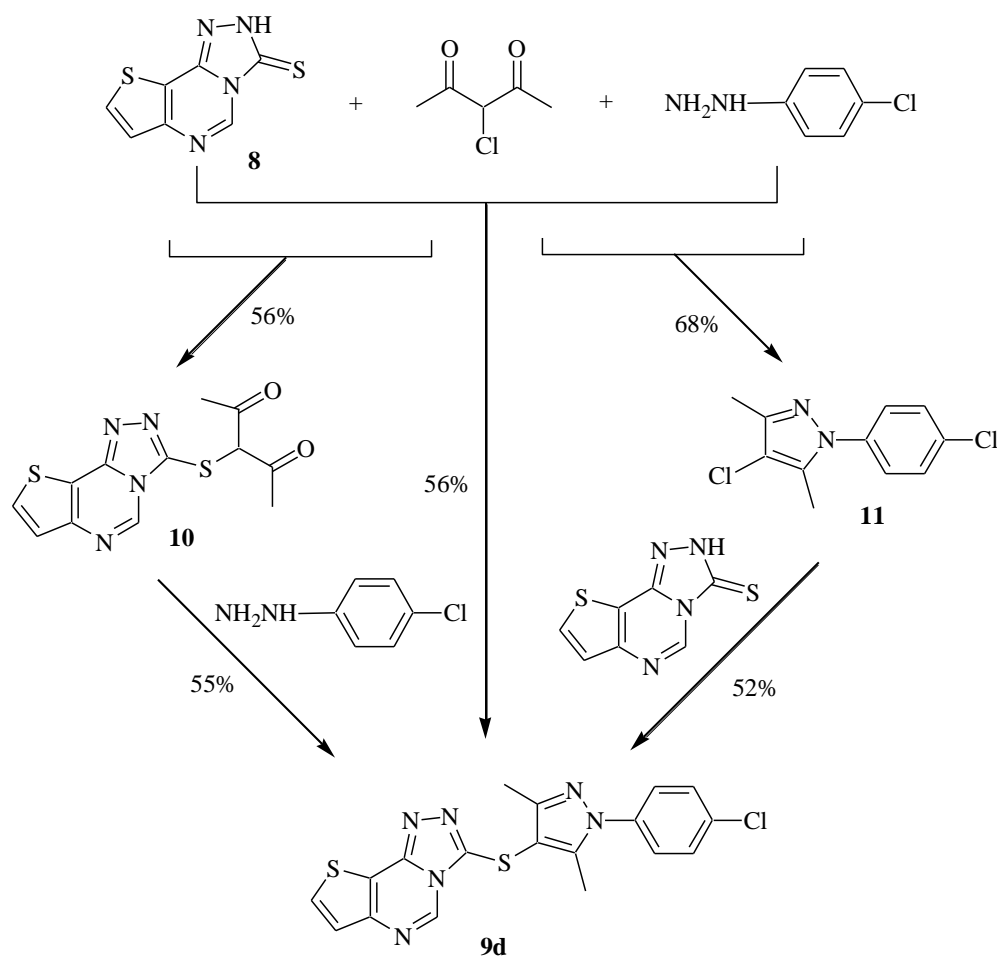
Entry	R	Yield (%) ^a	Entry	R	Yield (%) ^a
7a	Ph	56	9a	Ph	65
7b	2-Cl-C ₆ H ₄ -	61	9b	2-Cl-C ₆ H ₄ -	62
7c	3-Cl-C ₆ H ₄ -	55	9c	3-Cl-C ₆ H ₄ -	55
7d	4-Cl-C ₆ H ₄ -	70	9d	4-Cl-C ₆ H ₄ -	67
7e	4-Br-C ₆ H ₄ -	62	9e	4-Br-C ₆ H ₄ -	51
7f	4-F-C ₆ H ₄ -	44	9f	4-F-C ₆ H ₄ -	48
7g	4-MeO-C ₆ H ₄ -	56	9g	4-MeO-C ₆ H ₄ -	60

^a isolated yields



Scheme 2. Synthesis of triheterocyclic compounds in one-pot reaction

The structure of all new synthesized compounds was evident from their elemental analysis, mass spectra and ^1H NMR spectra. The results of diheterocyclic compounds **7a-g** and **9a-g** were summarized in Table 1. For the synthesis of triheterocyclic compounds **7h-i** and **9h-i** containing thienopyrimidinylpyrazole moiety, two thienopyrimidinylhydrazines were utilized in place of phenylhydrazine in one-pot reaction as shown in Scheme 2. The structure of **7h-i** and **9h-i** was established by elemental analysis, mass spectra, ^1H NMR and IR spectra. It is noteworthy that the ^1H NMR signals of these compounds showed four doublet signals ($J = 5.9$ Hz) because of two thiophene protons, and two singlet signals attributed to two pyrimidine protons in low field.



Scheme 3. Proposed mechanism for the formation of **9d** in one-pot reaction

The suggested mechanism for the conversion of reaction mixture to product **9d** in one-pot reaction, for instance, involves the initial formation of **10** and **11** from two different reactants through a simple substitution or imine formation-condensation reaction (Scheme 3). Progress of the subsequent reaction via fulfillment of condensation or substitution in the intermediates **10** and **11** gave the final product **9d** in 56% yield. In order to elucidate the proposed mechanism, we have first prepared **10** and **11** from different

two reactants, separately, and these compounds were subjected to react with 4-chlorophenylhydrazine and **8** under the same reaction conditions, respectively. The overall yield did not exceed 40% in step-by-step reaction by optimization of reaction condition. All of the spectral data and physical properties of the products obtained from these two-step strategies by two routes and the products of the one-pot strategy were identical. The intermediates **10** and **11** were also identified in reaction mixture of one-pot synthesis. Compared to step-by-step reaction, the present one-pot method has advantages of good yields, short reaction times and experimental simplicity. The compounds **7a-i** and **9a-i** were examined preliminarily for the antibacterial activity *in vitro* against *Escherichia coli* and *Staphylococcus aureus*. Some of them exhibited moderate activities. They are under evaluation for other biological activities and the results will be published elsewhere.

In conclusion, we have reported a simple and efficient method for the synthesis of new sulfur-linked heterocyclic compounds **7a-i** and **9a-i** with potential biological activities.

EXPERIMENTAL

Melting points were determined in capillary tubes on Büchi apparatus and are uncorrected. Each compound of the reactions was checked on thin-layer chromatography of Merck Kieselgel 60F₂₅₄ and purified by column chromatography Merck silica gel (70-230 mesh). The ¹H NMR spectra were recorded on Bruker DRX-300 FT NMR spectrometer (300 MHz) with Me₄Si as internal standard and chemical shifts are given in ppm (δ). IR spectra were recorded using an EXCALIBUR FTS-3000 FT IR spectrophotometer. Electron ionization mass spectra were recorded on a HP 59580 B spectrometer. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer.

General procedure for the preparation of 7a-i and 9a-i. A suspension of thieno[1,2,4]triazolo[4,3-*c*]pyrimidine-3(2*H*)-thione **6** or **8** (0.50 g, 2.40 mmol) and potassium hydroxide (0.27 g, 4.80 mmol) in EtOH (10 mL) was stirred at rt for 0.5 h. To this mixture 3-chloropentane-2,4-dione (0.32 g, 2.40 mmol), appropriate hydrazine (2.40 mmol) were added and it was allowed to stir at reflux for 8 h. The solution was cooled to rt and evaporated under reduced pressure. The residue was extracted with EtOAc and the extract was washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The solid product was purified by recrystallization from EtOH.

3-(3,5-Dimethyl-1-phenyl-1*H*-pyrazol-4-ylthio)thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (**7a**)

Mp 167-169 °C; IR (KBr) 1625 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.62 (s, 1H, pyrimidine), 8.15 (d, *J* = 5.9 Hz, 1H, thiophene), 7.85 (d, *J* = 5.9 Hz, 1H, thiophene), 7.12-6.88 (m, 5H, Ar), 2.14 (s, 6H); MS: (*m/z*) 378 (M⁺), 354, 208, 147, 135, 106, 77. *Anal.* Calcd for C₁₈H₁₄N₆S₂: C, 57.12; H, 3.73; N, 22.20. Found: C, 57.30; H, 3.60; N, 22.42.

3-[1-(2-Chlorophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7b)

Mp 171-173 °C; IR (KBr) 1631 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.61 (s, 1H, pyrimidine), 8.08 (d, *J* = 5.9 Hz, 1H, thiophene), 7.81 (d, *J* = 5.9 Hz, 1H, thiophene), 7.39 (d, 1H, Ar), 7.37 (d, 1H, Ar), 7.17 (t, 1H, Ar), 6.78 (t, 1H, Ar), 2.08 (s, 6H); MS: (m/z) 412 (M⁺), 388, 208, 140, 135, 111, 99. *Anal.* Calcd for C₁₈H₁₃ClN₆S₂: C, 52.36; H, 3.17; N, 20.35. Found: C, 52.22; H, 3.29; N, 20.21.

3-[1-(3-Chlorophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7c)

Mp 176-178 °C; IR (KBr) 1630 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.63 (s, 1H, pyrimidine), 8.08 (d, *J* = 5.9 Hz, 1H, thiophene), 7.81 (d, *J* = 5.9 Hz, 1H, thiophene), 7.17 (t, 1H, Ar), 7.08 (s, 1H, Ar), 7.00 (d, 1H, Ar), 6.72 (d, 1H, Ar), 2.05 (s, 6H); MS: (m/z) 412 (M⁺), 388, 208, 140, 135, 111, 99. *Anal.* Calcd for C₁₈H₁₃ClN₆S₂: C, 52.36; H, 3.17; N, 20.35. Found: C, 52.29; H, 3.25; N, 20.44.

3-[1-(4-Chlorophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7d)

Mp 168-169 °C; IR (KBr) 1633 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.64 (s, 1H, pyrimidine), 8.09 (d, *J* = 5.9 Hz, 1H, thiophene), 7.82 (d, *J* = 5.9 Hz, 1H, thiophene), 7.19 (d, 2H, Ar), 7.06 (d, 2H, Ar), 2.03 (s, 6H); MS: (m/z) 412 (M⁺), 388, 208, 140, 135, 111, 99. *Anal.* Calcd for C₁₈H₁₃ClN₆S₂: C, 52.36; H, 3.17; N, 20.35. Found: C, 52.19; H, 3.29; N, 20.24.

3-[1-(4-Bromophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7e)

Mp 173-175 °C; IR (KBr) 1626 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.63 (s, 1H, pyrimidine), 8.10 (d, *J* = 5.9 Hz, 1H, thiophene), 7.82 (d, *J* = 5.9 Hz, 1H, thiophene), 7.30 (d, 2H, Ar), 7.02 (d, 2H, Ar), 2.02 (s, 6H); MS: (m/z) 456 (M⁺), 434, 220, 208, 186, 184, 157, 155, 145, 135. *Anal.* Calcd for C₁₈H₁₃BrN₆S₂: C, 47.27; H, 2.86; N, 18.37. Found: C, 47.40; H, 2.84; N, 18.20.

3-[1-(4-Fluorophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7f)

Mp 208-210 °C; IR (KBr) 1630 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.67 (s, 1H, pyrimidine), 8.15 (d, *J* = 5.9 Hz, 1H, thiophene), 7.85 (d, *J* = 5.9 Hz, 1H, thiophene), 7.01 (d, 2H, Ar), 6.93 (d, 2H, Ar), 2.03 (s, 6H); MS: (m/z) 396 (M⁺), 375, 277, 216, 208, 136, 97, 66. *Anal.* Calcd for C₁₈H₁₃FN₆S₂: C, 54.53; H, 3.30; N, 21.20. Found: C, 54.42; H, 3.21; N, 21.32.

3-[1-(4-Methoxyphenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7g)

Mp 158-160 °C; IR (KBr) 1633 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.63 (s, 1H, pyrimidine), 8.10 (d, *J* = 5.9

Hz, 1H, thiophene), 7.80(d, $J = 5.9$ Hz, 1H, thiophene), 7.09 (d, 2H, Ar), 6.90 (d, 2H, Ar), 3.75 (s, 3H), 2.06 (s, 6H); MS: (m/z) 408 (M^+), 384, 208, 135, 111. *Anal.* Calcd for $C_{19}H_{16}N_6OS_2$: C, 55.86; H, 3.95; N, 20.57. Found: C, 56.11; H, 3.99; N, 20.79.

3-[3,5-Dimethyl-1-(thieno[2,3-*d*]pyrimidin-4-yl)-1*H*-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7h)

Mp 151-154 °C; IR (KBr) 1625 cm^{-1} ; 1H NMR (DMSO- d_6): δ 9.60 (s, 1H, pyrimidine), 8.45 (s, 1H, pyrimidine), 8.16 (d, $J = 5.9$ Hz, 1H, thiophene), 8.08 (d, $J = 5.9$ Hz, 1H, thiophene), 7.81 (d, $J = 5.9$ Hz, 1H, thiophene), 7.62 (d, $J = 5.9$ Hz, 1H, thiophene), 2.22 (s, 6H); MS: (m/z) 436 (M^+), 412, 208, 205, 191, 164, 135, 123, 109, 79, 64. *Anal.* Calcd for $C_{18}H_{12}N_8S_3$: C, 49.52; H, 2.77; N, 25.67. Found: C, 49.31; H, 2.62; N, 25.79.

3-[3,5-Dimethyl-1-(thieno[3,2-*d*]pyrimidin-4-yl)-1*H*-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (7i)

Mp 193-194 °C; IR (KBr) 1620 cm^{-1} ; 1H NMR (DMSO- d_6): δ 9.59 (s, 1H, pyrimidine), 8.48 (s, 1H, pyrimidine), 8.30 (d, $J = 5.9$ Hz, 1H, thiophene), 8.13 (d, $J = 5.9$ Hz, 1H, thiophene), 7.80 (d, $J = 5.9$ Hz, 1H, thiophene), 7.73 (d, $J = 5.9$ Hz, 1H, thiophene), 2.19 (s, 6H); MS: (m/z) 436 (M^+), 208, 191, 135, 109, 79. *Anal.* Calcd for $C_{18}H_{12}N_8S_3$: C, 49.52; H, 2.77; N, 25.67. Found: C, 49.44; H, 2.60; N, 25.55.

3-(3,5-Dimethyl-1-phenyl-1*H*-pyrazol-4-ylthio)thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9a)

Mp 177-179 °C; IR (KBr) 1630 cm^{-1} ; 1H NMR (DMSO- d_6): δ 9.58 (s, 1H, pyrimidine), 8.30 (d, $J = 5.9$ Hz, 1H, thiophene), 7.71 (d, $J = 5.9$ Hz, 1H, thiophene), 7.15-6.90 (m, 5H, Ar), 1.98 (s, 6H); MS: (m/z) 378 (M^+), 354, 208, 135, 106, 77, 65. *Anal.* Calcd for $C_{18}H_{14}N_6S_2$: C, 57.12; H, 3.73; N, 22.20. Found: C, 57.01; H, 3.66; N, 22.30.

3-[1-(2-Chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9b)

Mp 176-178 °C; IR (KBr) 1633 cm^{-1} ; 1H NMR (DMSO- d_6): δ 9.57 (s, 1H, pyrimidine), 8.26 (d, $J = 5.9$ Hz, 1H, thiophene), 7.66 (d, $J = 5.9$ Hz, 1H, thiophene), 7.35 (d, 1H, Ar), 7.26 (d, 1H, Ar), 7.14 (t, 1H, Ar), 6.73 (t, 1H, Ar), 2.04 (s, 6H); MS: (m/z) 412 (M^+), 388, 262, 208, 181, 140, 135, 111, 99. *Anal.* Calcd for $C_{18}H_{13}ClN_6S_2$: C, 52.36; H, 3.17; N, 20.35. Found: C, 52.30; H, 3.08; N, 20.28.

3-[1-(3-Chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9c)

Mp 153-155 °C; IR (KBr) 1631 cm^{-1} ; 1H NMR (DMSO- d_6): δ 9.58 (s, 1H, pyrimidine), 8.26 (d, $J = 5.9$ Hz, 1H, thiophene), 7.67 (d, $J = 5.9$ Hz, 1H, thiophene), 7.10 (t, 1H, Ar), 7.00 (s, 1H, Ar), 6.92 (d, 1H, Ar), 6.66 (d, 1H, Ar), 1.97 (s, 6H); MS: (m/z) 412 (M^+), 388, 208, 181, 162, 140, 135, 111, 99. *Anal.* Calcd for $C_{18}H_{13}ClN_6S_2$: C, 52.36; H, 3.17; N, 20.35. Found: C, 52.28; H, 3.21; N, 20.47.

3-[1-(4-Chlorophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9d)

Mp 93-95 °C; IR (KBr) 1635 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.54 (s, 1H, pyrimidine), 8.24 (d, *J* = 5.9 Hz, 1H, thiophene), 7.65 (d, *J* = 5.9 Hz, 1H, thiophene), 7.19 (d, 2H, Ar), 7.06 (d, 2H, Ar), 2.03 (s, 6H); MS: (m/z) 412 (M⁺), 388, 264, 222, 208, 177, 135, 111, 99. *Anal.* Calcd for C₁₈H₁₃ClN₆S₂: C, 52.36; H, 3.17; N, 20.35. Found: C, 52.28; H, 3.05; N, 20.41.

3-[1-(4-Bromophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9e)

Mp 106-108 °C; IR (KBr) 1626 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.61 (s, 1H, pyrimidine), 8.32 (d, *J* = 5.9 Hz, 1H, thiophene), 7.73 (d, *J* = 5.9 Hz, 1H, thiophene), 7.33 (d, 2H, Ar), 7.04 (d, 2H, Ar), 2.03 (s, 6H); MS: (m/z) 456 (M⁺), 222, 208, 185, 171, 155, 135, 91. *Anal.* Calcd for C₁₈H₁₃BrN₆S₂: C, 47.27; H, 2.86; N, 18.37. Found: C, 47.17; H, 2.77; N, 18.44.

3-[1-(4-Fluorophenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9f)

Mp 124-126 °C; IR (KBr) 1630 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.55 (s, 1H, pyrimidine), 8.25 (d, *J* = 5.7 Hz, 1H, thiophene), 7.65 (d, *J* = 5.7 Hz, 1H, thiophene), 7.02 (d, 2H, Ar), 6.94 (d, 2H, Ar), 1.96 (s, 6H); MS: (m/z) 396 (M⁺), 375, 277, 216, 208, 136, 97. *Anal.* Calcd for C₁₈H₁₃FN₆S₂: C, 54.53; H, 3.30; N, 21.20. Found: C, 54.59; H, 3.23; N, 21.29.

3-[1-(4-Methoxyphenyl)-3,5-dimethyl-1H-pyrazol-4-ylthio]thieno[3,2-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9g)

Mp 113-115 °C; IR (KBr) 1633 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.58 (s, 1H, pyrimidine), 8.31 (d, *J* = 5.9 Hz, 1H, thiophene), 7.73 (d, *J* = 5.9 Hz, 1H, thiophene), 7.11 (d, 2H, Ar), 6.94 (d, 2H, Ar), 3.72 (s, 3H), 2.06 (s, 6H); MS: (m/z) 408 (M⁺), 384, 208, 164, 135, 111. *Anal.* Calcd for C₁₉H₁₆N₆OS₂: C, 55.86; H, 3.95; N, 20.57. Found: C, 55.74; H, 3.82; N, 20.69.

3-[3,5-Dimethyl-1-(thieno[2,3-*d*]pyrimidin-4-yl)-1H-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9h)

Mp 165-167 °C; IR (KBr) 1630 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.53 (s, 1H, pyrimidine), 8.40 (s, 1H, pyrimidine), 8.24 (d, *J* = 5.9 Hz, 1H, thiophene), 8.08 (d, *J* = 5.9 Hz, 1H, thiophene), 7.66 (d, *J* = 5.9 Hz, 1H, thiophene), 7.51 (d, *J* = 5.9 Hz, 1H, thiophene), 2.13 (s, 6H); MS: (m/z) 436 (M⁺), 208, 191, 164, 135, 109. *Anal.* Calcd for C₁₈H₁₂N₈S₃: C, 49.52; H, 2.77; N, 25.67. Found: C, 49.42; H, 2.66; N, 25.60.

3-[3,5-Dimethyl-1-(thieno[3,2-*d*]pyrimidin-4-yl)-1H-pyrazol-4-ylthio]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (9i)

Mp 203-204 °C; IR (KBr) 1625 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 9.59 (s, 1H, pyrimidine), 8.50 (s, 1H,

pyrimidine), 8.30 (d, $J = 5.9$ Hz, 1H, thiophene), 8.19 (d, $J = 5.9$ Hz, 1H, thiophene), 7.77 (d, $J = 5.9$ Hz, 1H, thiophene), 7.70 (d, $J = 5.9$ Hz, 1H, thiophene), 2.18 (s, 6H); MS: (m/z) 436 (M^+), 208, 191, 135, 109. *Anal.* Calcd for $C_{18}H_{12}N_8S_3$: C, 49.52; H, 2.77; N, 25.67. Found: C, 49.66; H, 2.60; N, 25.77.

3-(Thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidin-3-ylthio)pentane-2,4-dione (10)

Mp 149-151 °C; IR (KBr) 1726 cm^{-1} ; 1H NMR (DMSO- d_6): δ 9.57 (s, 1H, pyrimidine), 8.26 (d, $J = 5.9$ Hz, 1H, thiophene), 7.64 (d, $J = 5.9$ Hz, 1H, thiophene), 2.44 (s, 6H); MS: (m/z) 306 (M^+), 208, 162, 135, 123, 94. *Anal.* Calcd for $C_{12}H_{10}N_4O_2S_2$: C, 47.04; H, 3.29; N, 18.29. Found: C, 47.10; H, 3.15; N, 18.40.

4-Chloro-1-(4-chlorophenyl)-3,5-dimethyl-1*H*-pyrazole (11)¹⁶

Mp 74-75 °C; IR (KBr) 1640 cm^{-1} ; 1H NMR (DMSO- d_6): δ 7.58-7.56 (m, 4H, Ar), 2.29 (s, 3H), 2.19 (s, 3H).

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