

Anna Hovhannisyan*, Lilit Aristakesyan and Gagik Melikyan

Facile approach to the synthesis of substituted thieno[2,3-*d*]pyrimidin-4-ones

Abstract: Condensation of Gewald's thiophenes substituted with a dimethylaminomethyleneamino group at position 2 with primary amines yields 5/6-aryl-thieno[2,3-*d*]pyrimidin-4-ones with variable substituents at the N3 position.

Keywords: amines; cyclocondensation; enamines; Gewald's reaction; thieno[2,3-*d*]pyrimidin-4-ones.

*Corresponding author: Anna Hovhannisyan, Yerevan State University, Alex Manoogian 1, 0025 Yerevan, Armenia, e-mail: annahovh@gmail.com

Lilit Aristakesyan: Yerevan State University, Alex Manoogian 1, 0025 Yerevan, Armenia

Gagik Melikyan: Yerevan State University, Alex Manoogian 1, 0025 Yerevan, Armenia

Introduction

Thienopyrimidines have been shown to possess a variety of pharmacological activities including analgesic, anti-inflammatory, antipyretic, antimicrobial, anticonvulsant, fungicidal, and antiplatelet properties (Ibrahim et al., 1996; Varvounis and Giannopoulos, 1996). Several derivatives are also central nervous system agents (Sharma et al., 2010) and inhibitors of Cyclin D1-CDK4 (Horiuchi et al., 2009). Several 6-(4-chlorophenyl)-3-substituted thieno[3,2-*d*]pyrimidin-4(3*H*)-ones with aromatic and heterocyclic substituents are melanin-concerning hormone receptor agonists (Tavares et al., 2006). Earlier we described a convenient method for synthesis of thieno[2,3-*d*]pyrimidin-4-ones substituted with aliphatic groups (Hovhannisyan et al., 2004) at the ring atom N3. Now we enhance this chemistry by the synthesis of 5- and 6-aromatically substituted derivatives **3a–s** (Scheme 1).

Results and discussion

Readily available Gewald's 2-aminothiophenes **1a–e** were allowed to react with *N,N'*-dimethylformamide dimethylacetal (DMF/DMA) in boiling anhydrous xylenes to give

the corresponding new dimethylaminomethyleneamino derivatives **2a–e** in high yields (up to 97%).

A subsequent treatment of the intermediate products **2** with primary amines in xylenes under reflux conditions furnished substituted thieno[2,3-*d*]pyrimidin-4-ones **3a–r** with yields up to 87%. The highest yields were obtained with the 1:3 molar ratio of the intermediate product **2** to the primary amine. Elimination of gaseous dimethylamine was used to monitor the progress of the reaction. The first step of this synthesis apparently involves addition of the amine to the methyleneamino functionality of **2**. The observed high yields of the final products **3** show that a possible reaction of the amine with the ester function of **2** is not a problem.

The products **3a–r** contain a substituted alkyl group at the ring position N3. This group is derived from the aliphatic amine. The synthesis of an aromatic analog **3s** by the reaction of **2b** with *p*-anisidine required the use of acetic acid as a solvent. Product **3s** was obtained in low yield, and attempted reactions with other anilines were not successful.

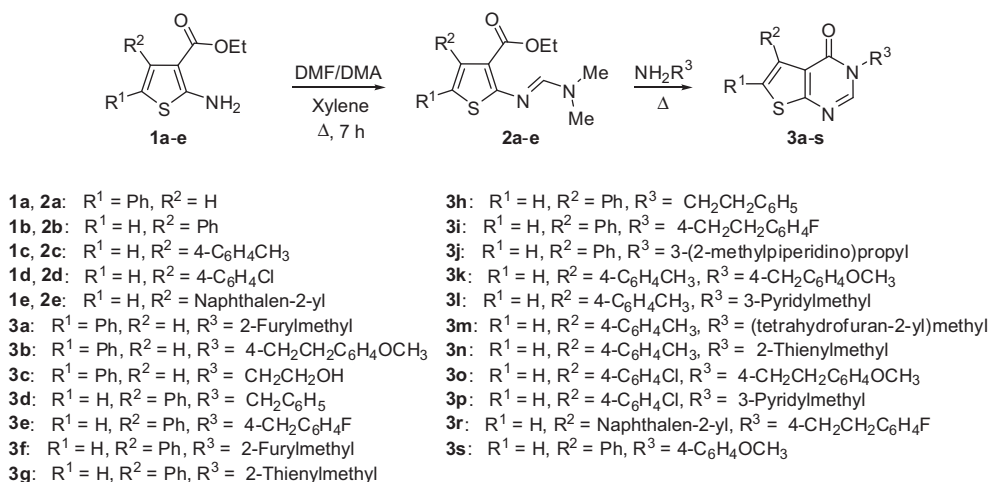
Conclusions

Readily available enamines **2** are useful intermediate products in the synthesis of substituted thieno[2,3-*d*]pyrimidin-4-ones **3** that contain a primary group at the N3 position.

Experimental section

General

Melting points were determined on an SMP-10 melting point apparatus and are uncorrected. ¹H NMR spectra were obtained on a Varian Mercury 300 VX spectrometer at 300 MHz with tetramethylsilane as internal reference in DMSO-*d*₆ solution at 303 K. Thin layer chromatography analysis was performed on Silufol-250 UV plates eluting with acetone/benzene (1:3); detection was with UV light at 254 nm and iodine vapors. The 2-aminothiophene **1a** was synthesized by 3-component Gewald's reaction of phenylacetaldehyde, ethyl cyanoacetate,



Scheme 1 The synthesis of substituted thieno[2,3-*d*]pyrimidin-4-ones.

and sulfur. The 2-component reaction with arylidenecyanoacetates was used in the preparation of compounds **1b–e**, as described previously (Gewald, 1966).

General procedure for synthesis of ethyl

2-(Dimethylaminomethyleneamino)thiophene-3-carboxylates 2a–e A mixture of a thiophene **1a–e** (10 mmol) and DMF/DMA (1.56 mL, 12 mmol) in anhydrous xylenes (20 mL) was heated under reflux for 7 h. After cooling to room temperature 5 mL of light petroleum was added, and the precipitated crystals of **2a–e** were filtered, washed with diethyl ether, and dried.

Ethyl 2-(dimethylaminomethyleneamino)-5-phenyl-thiophene-3-carboxylate (2a) Yield 94%; mp 80°C; ^1H NMR: δ 1.05 (t, $J = 7.1$ Hz, 3H), 3.04 (s, 3H), 3.11 (s, 3H), 4.01 (q, $J = 7.1$ Hz, 2H), 6.44 (s, 1H), 7.15–7.38 (m, 5H), 7.76 (s, 1H). Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$: C, 63.55; H, 6.00; N, 9.26; S, 10.60. Found: C, 63.12; H, 6.03; N, 9.14; S, 10.48.

Ethyl 2-(dimethylaminomethyleneamino)-4-phenylthiophene-3-carboxylate (2b) Yield 95%; mp 95°C; ^1H NMR: δ 1.05 (t, $J = 7.1$ Hz, 3H), 3.04 (s, 3H), 3.11 (s, 3H), 4.03 (q, $J = 7.1$ Hz, 2H), 6.48 (s, 1H), 7.17–7.37 (m, 5H), 7.73 (s, 1H). Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$: C, 63.55; H, 6.00; N, 9.26; S, 10.60. Found: C, 63.16; H, 5.92; N, 9.15; S, 10.48.

Ethyl 2-(dimethylaminomethyleneamino)-4-*p*-tolylthiophene-3-carboxylate (2c) Yield 92%; mp 75°C; ^1H NMR: δ 1.09 (t, $J = 7.1$ Hz, 3H), 2.36 (s, 3H), 3.02 (s, 3H), 3.11 (s, 3H), 4.04 (q, $J = 7.1$ Hz, 2H), 6.45 (s, 1H), 7.03–7.20 (m, 4H), 7.71 (s, 1H). Anal. Calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$: C, 64.53; H, 6.37; N, 8.85; S, 10.13. Found: C, 64.30; H, 6.28; N, 8.76; S, 9.95.

Ethyl 4-(4-chlorophenyl)-2-(dimethylaminomethyleneamino)thiophene-3-carboxylate (2d) Yield 92%; mp 98°C; ^1H NMR: δ 1.10 (t, $J = 7.1$ Hz, 3H), 3.03 (s, 3H), 3.11 (s, 3H), 4.04 (q, $J = 7.1$ Hz, 2H), 6.51 (s, 1H), 7.20–7.32 (m, 4H), 7.72 (s, 1H). Anal. Calcd for $\text{C}_{16}\text{H}_{17}\text{ClN}_2\text{O}_2\text{S}$:

C, 57.05; H, 5.09; Cl, 10.53; N, 8.32; S, 9.52. Found: C, 56.70; H, 5.02; Cl, 10.40; N, 8.24; S, 9.41.

Ethyl 2-(dimethylaminomethyleneamino)-4-(naphthalen-2-yl)thiophene-3-carboxylate (2e) Yield 95%; mp 104°C; ^1H NMR: δ 1.02 (t, $J = 7.1$ Hz, 3H), 3.05 (s, 3H), 3.13 (s, 3H), 4.03 (q, $J = 7.1$ Hz, 2H), 6.62 (s, 1H), 7.38–7.46 (m, 3H), 7.73–7.84 (m, 5H). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$: C, 68.16; H, 5.72; N, 7.95; S, 9.10. Found: C, 67.80; H, 5.65; N, 7.83; S, 8.98.

General procedure for the synthesis of substituted thieno[2,3-*d*]pyrimidin-4(3*H*)-ones 3a–r

A mixture of **2a–e** (5 mmol) and primary amine (15 mmol) in anhydrous xylenes (20 mL) was heated under reflux for 30 h. After cooling to room temperature the solution was treated with 8 mL of light petroleum. The precipitated crystals of **3a–r** were filtered, washed with diethyl ether, and dried under reduced pressure.

3-(2-Furylmethyl)-6-phenylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (3a) Yield 53%; mp 200°C; IR: 1657, 1688 cm^{-1} ; ^1H NMR: δ 5.23 (s, 2H), 6.35 (dd, $J = 3.1$ Hz, 1.9 Hz, 1H), 6.45 (dd, $J = 3.1$ Hz, 0.8 Hz, 1H), 7.28–7.35 (m, 1H), 7.35–7.43 (m, 2H), 7.44 (dd, $J = 1.9$ Hz, 0.8 Hz, 1H), 7.63–7.68 (m, 3H), 8.35 (s, 1H). Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_2\text{S}$: C, 66.22; H, 3.92; N, 9.08; S, 10.40. Found: C, 65.84; H, 3.84; N, 8.95; S, 10.36.

3-[2-(4-Methoxyphenyl)ethyl]-6-phenylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (3b) Yield 59%; mp 174°C; IR: 1650, 1696 cm^{-1} ; ^1H NMR: δ 2.97 (t, $J = 7.3$ Hz, 2H), 3.76 (s, 3H), 4.14–4.21 (t, $J = 7.3$ Hz, 2H), 6.76–6.83 (m, 2H), 7.10–7.15 (m, 2H), 7.28–7.45 (m, 3H), 7.65–7.70 (m, 2H), 7.70 (s, 1H), 8.02 (s, 1H). Anal. Calcd for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$: C, 69.59; H, 5.01; N, 7.73; S, 8.85. Found: C, 69.34; H, 4.93; N, 7.66; S, 8.76.

3-(2-Hydroxyethyl)-6-phenylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (3c) Yield 39%; mp 156°C; IR: 1655, 1693, 3302, 3363 cm^{-1} ; ^1H NMR:

δ 3.70 (q, $J = 5.2$ Hz, 2H), 4.07 (t, $J = 5.2$ Hz, 2H), 4.72 (t, $J = 5.2$ Hz, 1H), 7.31 (m, 1H), 7.41 (m, 2H), 7.66 (m, 2H), 7.66 (s, 1H); 8.16 (s, 1H). Anal. Calcd for $C_{14}H_{12}N_2O_2S$: C, 61.75; H, 4.44; N, 10.29; S, 11.77. Found: C, 61.53; H, 4.37; N, 10.20; S, 11.64.

3-Benzyl-5-phenyl-thieno[2,3-*d*]pyrimidin-4(3H)-one (3d) Yield 50%; mp 168°C; IR: 1661, 1697 cm^{-1} ; 1H NMR: δ 5.19 (s, 2H), 7.19–7.42 (m, 9H), 7.49 (dd, $J = 7.7$ Hz, 1.7 Hz, 2H), 8.51 (s, 1H). Anal. Calcd for $C_{19}H_{14}N_2OS$: C, 71.67; H, 4.43; N, 8.80; S, 10.07. Found: C, 71.27; H, 4.38; N, 8.62; S, 10.00.

3-(4-Fluorobenzyl)-5-phenylthieno[2,3-*d*]pyrimidin-4(3H)-one (3e) Yield 72%; mp 171°C; IR: 1647, 1698 cm^{-1} ; 1H NMR: δ 5.16 (s, 2H), 6.97–7.07 (m, 2H), 7.23 (s, 1H), 7.29–7.39 (m, 3H), 7.43–7.52 (m, 4H), 8.56 (s, 1H). Anal. Calcd for $C_{19}H_{13}FN_2OS$: C, 67.84; H, 3.90; F, 5.65; N, 8.33; S, 9.53. Found: C, 67.46; H, 3.91; F, 5.59; N, 8.22; S, 9.42.

3-(2-Furylmethyl)-5-phenylthieno[2,3-*d*]pyrimidin-4(3H)-one (3f) Yield 67%; mp 181°C; IR: 1652, 1690 cm^{-1} ; 1H NMR: δ 5.19 (s, 2H, CH_2), 6.33 (dd, $J = 3.2$ Hz, 1.9 Hz, 1H), 6.42 (dd, $J = 3.2$ Hz, 0.8 Hz, 1H), 7.22 (s, 1H), 7.30–7.38 (m, 3H), 7.43 (dd, $J = 1.9$ Hz, 0.8 Hz, 1H), 7.45–7.51 (m, 2H), 8.40 (s, 1H). Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.22; H, 3.92; N, 9.08; S, 10.40. Found: C, 65.75; H, 3.85; N, 9.03; S, 10.28.

5-Phenyl-3-(2-thienylmethyl)thieno[2,3-*d*]pyrimidin-4(3H)-one (3g) Yield 65%; mp 179°C; IR: 1659, 1697 cm^{-1} ; 1H NMR: δ 5.36 (s, 2H), 6.92 (dd, $J = 5.1$ Hz, 3.5 Hz, 1H), 7.20 (dd, $J = 3.5$ Hz, 1.1 Hz, 1H), 7.24 (s, 1H), 7.27 (dd, $J = 5.1$ Hz, 1.1 Hz, 1H), 7.30–7.40 (m, 3H), 7.48–7.54 (m, 2H), 8.53 (s, 1H). Anal. Calcd for $C_{17}H_{12}N_2OS_2$: C, 62.94; H, 3.73; N, 8.63; S, 19.77. Found: C, 62.63; H, 3.74; N, 8.55; S, 19.64.

3-Phenethyl-5-phenylthieno[2,3-*d*]pyrimidin-4(3H)-one (3h) Yield 45%; mp 128°C; IR: 1662, 1688 cm^{-1} ; 1H NMR: δ 2.94–3.08 (m, 2H), 4.12–4.28 (m, 2H), 7.15–7.32 (m, 6H), 7.31–7.41 (m, 3H), 7.48–7.54 (m, 2H), 8.12 (s, 1H). Anal. Calcd for $C_{20}H_{16}N_2OS$: C, 72.26; H, 4.85; N, 8.43; S, 9.65. Found: C, 72.02; H, 4.80; N, 8.36; S, 9.68.

3-[2-(4-Fluorophenyl)ethyl]-5-phenylthieno[2,3-*d*]pyrimidin-4(3H)-one (3i) Yield 53%; mp 143°C; IR: 1660, 1695 cm^{-1} ; 1H NMR: δ 2.96–3.03 (m, 2H), 4.17 (dd, $J = 8.3$ Hz, 6.8 Hz, 2H), 6.94–7.05 (m, 2H), 7.21 (s, 1H), 7.22–7.28 (m, 2H), 7.30–7.40 (m, 3H), 7.48–7.53 (m, 2H), 8.15 (s, 1H). Anal. Calcd for $C_{20}H_{15}FN_2OS$: C, 68.55; H, 4.31; F, 5.42; N, 7.99; S, 9.15. Found: C, 68.17; H, 4.25; F, 5.36; N, 8.03; S, 9.05.

3-[3-(2-Methylpiperidino)propyl]-5-phenylthieno[2,3-*d*]pyrimidin-4(3H)-one (3j) Yield 57%; mp 73°C; IR: 1647, 1696 cm^{-1} ; 1H NMR: δ 1.00 (d, $J = 6.3$ Hz, 3H), 1.28 (m, 2H), 1.44–1.65 (m, 4H), 1.75–1.95 (m, 2H), 2.03 (ddd, $J = 11.4$ Hz, 9.2 Hz, 3.5 Hz, 1H), 2.20 (m, 1H), 2.28 (m, 1H), 2.69–2.77 (m, 2H), 3.93 (m, 1H), 4.03 (m, 1H), 7.20 (s, 1H), 7.29–7.38 (m, 3H), 7.46–7.51 (m, 2H), 8.29 (s, 1H). Anal. Calcd for $C_{21}H_{25}N_3OS$: C, 68.63; H, 6.86; N, 11.43; S, 8.72. Found: C, 68.31; H, 6.81; N, 11.37; S, 8.61.

3-(4-Methoxybenzyl)-5-*p*-tolylthieno[2,3-*d*]pyrimidin-4(3H)-one (3k) Yield 72%; mp 140°C; IR: 1651, 1693 cm^{-1} ; 1H NMR: δ 2.40 (s, 3H), 3.75 (s, 3H), 5.09 (s, 2H), 6.77–6.84 (m, 2H), 7.11–7.18 (m, 3H), 7.29–7.40 (m, 4H), 8.46 (s, 1H). Anal. Calcd for $C_{21}H_{18}N_2O_2S$: C, 69.59; H, 5.01; N, 7.73; S, 8.85. Found: C, 69.45; H, 5.04; N, 7.61; S, 8.80.

3-(3-Pyridylmethyl)-5-*p*-tolylthieno[2,3-*d*]pyrimidin-4(3H)-one (3l) Yield 55%; mp 145°C; IR: 1657, 1689 cm^{-1} ; 1H NMR: δ 2.38 (s, 3H), 5.23 (s, 2H), 7.11 (m, 2H), 7.14 (s, 1H), 7.22 (ddd, $J = 7.6$ Hz, 4.8 Hz, 1.2 Hz, 1H), 7.34 (m, 2H), 7.37 (dt, $J = 7.8$ Hz, 1.1 Hz, 1H), 7.69 (ddd, $J = 7.8$ Hz, 1.8 Hz, 1H), 8.43 (s, 1H), 8.48 (ddd, $J = 4.8$ Hz, 1.8 Hz, 1.1 Hz, 1H). Anal. Calcd for $C_{19}H_{15}N_3OS$: C, 68.45; H, 4.53; N, 12.60; S, 9.62. Found: C, 68.31; H, 4.56; N, 12.51; S, 9.51.

[3-(Tetrahydrofuran-2-yl)methyl]-5-*p*-tolylthieno[2,3-*d*]pyrimidin-4(3H)-one (3m) Yield 76%; mp 117°C; IR: 1648, 1691 cm^{-1} ; 1H NMR: δ 1.54–1.67 (m, 1H), 1.80–2.10 (m, 3H), 2.40 (s, 3H), 3.65–3.76 (m, 1H), 3.76–3.90 (m, 2H), 4.05–4.15 (m, 1H), 4.23 (dd, $J = 13.4$ Hz, 3.1 Hz, 1H), 7.10–7.16 (m, 3H), 7.34–7.40 (m, 2H), 8.18 (s, 1H). Anal. Calcd for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.56; N, 8.58; S, 9.82. Found: C, 65.83; H, 5.49; N, 8.48; S, 9.71.

3-(2-Thienylmethyl)-5-*p*-tolylthieno[2,3-*d*]pyrimidin-4(3H)-one (3n) Yield 72%; mp 178°C; IR: 1645, 1690 cm^{-1} ; 1H NMR: δ 2.41 (s, 3H), 5.35 (s, 2H), 6.92 (dd, $J = 5.1$ Hz, 3.5 Hz, 1H), 7.13–7.18 (m, 3H), 7.20 (dd, $J = 3.5$ Hz, 1.1 Hz, 1H), 7.26 (dd, $J = 5.1$ Hz, 1.1 Hz, 1H), 7.36–7.41 (m, 2H), 8.50 (s, 1H). Anal. Calcd for $C_{18}H_{14}N_2OS_2$: C, 63.88; H, 4.17; N, 8.28; S, 18.95. Found: C, 63.42; H, 4.02; N, 8.21; S, 18.79.

5-(4-Chlorophenyl)-3-(4-methoxyphenethyl)thieno[2,3-*d*]pyrimidin-4(3H)-one (3o) Yield 61%; mp 114°C; IR: 1657, 1691 cm^{-1} ; 1H NMR: δ 3.75 (s, 3H), 5.10 (s, 2H), 6.77–6.84 (m, 2H), 7.24 (s, 1H), 7.31–7.38 (m, 4H), 7.46–7.51 (m, 2H), 8.49 (s, 1H). Anal. Calcd for $C_{21}H_{17}ClN_2O_2S$: C, 63.55; H, 4.32; Cl, 8.93; N, 7.06; S, 8.08. Found: C, 63.13; H, 4.34; Cl, 8.88; N, 6.98; S, 8.02.

5-(4-Chlorophenyl)-3-[(3-pyridyl)methyl]thieno[2,3-*d*]pyrimidin-4(3H)-one (3p) Yield 47%; mp 145°C; IR: 1655, 1688 cm^{-1} ; 1H NMR: δ 5.24 (s, 2H), 7.22 (ddd, $J = 7.6$ Hz, 4.9 Hz, 1.0 Hz, 1H), 7.26 (s, 1H), 7.31 (m, 2H), 7.38 (dt, $J = 7.8$ Hz, 1.0 Hz, 1H), 7.46 (m, 2H), 7.70 (ddd, $J = 7.8$ Hz, 7.6 Hz, 1.8 Hz, 1H), 8.46 (s, 1H), 8.48 (ddd, $J = 4.9$ Hz, 1.8 Hz, 1.0 Hz, 1H). Anal. Calcd for $C_{18}H_{12}ClN_3OS$: C, 61.10; H, 3.42; Cl, 10.02; N, 11.88; S, 9.06. Found: C, 61.15; H, 3.39; Cl, 9.91; N, 11.76; S, 8.99.

3-(4-Fluorophenethyl)-5-(naphthalen-2-yl)thieno[2,3-*d*]pyrimidin-4(3H)-one (3r) Yield 61%; mp 110°C; IR: 1648, 1687 cm^{-1} ; 1H NMR: δ 3.00 (m, 2H), 4.19 (m, 2H), 6.99 (m, 2H), 7.25 (m, 2H), 7.35 (s, 1H), 7.44–7.51 (m, 2H), 7.65 (dd, $J = 8.5$ Hz, 1.8 Hz, 1H), 7.84 (d, $J = 8.5$ Hz, 1H), 7.83–7.91 (m, 2H), 7.99 (d, $J = 1.8$ Hz, 1H), 8.18 (s, 1H). Anal. Calcd for $C_{24}H_{17}FN_2OS$: C, 71.98; H, 4.28; F, 4.74; N, 6.99; S, 8.01. Found: C, 71.49; H, 4.25; F, 4.68; N, 6.91; S, 7.93.

Synthesis of 3-(4-methoxyphenyl)-5-phenylthieno[2,3-*d*]pyrimidin-4(3H)-one (3s) A mixture of **2b** (1g, 3.3 mmol) and *p*-anisidine (0.41 g, 3.3 mmol) in glacial acetic acid (10 mL) was heated under reflux for 30 h, then cooled and treated with 8 mL of light petroleum. The precipitated crystals of **3s** were filtered, washed with diethyl ether, and dried under reduced pressure: Yield 0.36 g (32%); mp 162°C; IR: 1642, 1691 cm^{-1} ; 1H NMR: δ 3.86 (s, 3H), 7.02 (d, $J = 8.9$ Hz, 2H), 7.37–7.24 (m, 6H), 7.50 (dd, $J = 7.5$ Hz, 1.7 Hz, 2H), 8.16 (s, 1H). Anal. Calcd for $C_{19}H_{14}N_2O_2S$: C, 68.25; H, 4.22; N, 8.38; S, 9.59. Found: C, 67.87; H, 4.15; N, 8.31; S, 9.52.

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References

- Gewald, K.; Schinke, E.; Bottcher, H. 2-Amino-thiophene aus methylenaktiven Nitrilen, Carbonylverbindungen und Schwefel. *Chem. Ber.* **1966**, *99*, 94–99.
- Hovhannisyan, A.; Melikyan, G.; Avetisyan, A. Republic of Armenia, patent #1469 A2, 6 July, 2004.
- Horiuchi, T.; Chiba, J.; Uoto, K.; Soga, T. Discovery of novel thieno[2,3-*d*]pyrimidin-4-yl hydrazone-based inhibitors of Cyclin D1-CDK4: synthesis, biological evaluation, and structure-activity relationships. *Bioorgan. Med. Chem. Lett.* **2009**, *19*, 305–308.
- Ibrahim, J. A.; Elwahy, A. H. M.; Kadry, A. M. Thienopyrimidines: synthesis, reactions and biological activity. *Adv. Heterocycl. Chem.* **1996**, *65*, 235–281.
- Sharma, C.; Terande, S.; Chavan, R.; Bhosale, A. V. Synthesis of thienopyrimidines and their antipsychotic activity. *E-J. Chem.* **2010**, *7*, 655–664 (<http://www.e-journals.net>).
- Tavares, F. X.; Al-Barazani, K. A.; Bishop, M. J.; Britt, C. S.; Carlton, D. L.; Cooper, J. P.; Feldman, P. L.; Garrido, D. M.; Goetz, A. S.; Grizzle, M. K.; Herzog, D. L.; Ignar, D. M.; Lang, D. G.; McIntyre, M. S.; Ott, R. J.; Peat, A. J.; Zhou, H.-Q. 6-(4-Chlorophenyl)-3-substitute-thieno[3,2-*d*]pyrimidin-4(3H)-one-based melanin-concerning hormone receptor agonist. *J. Med. Chem.* **2006**, *49*, 7108–7118.
- Varvounis, G.; Giannopoulos, T. Synthesis, chemistry and biological properties of thienopyrimidines. *Adv. Heterocycl. Chem.* **1996**, *66*, 193–283.