

Efficient synthesis and fungicidal activities of 2-alkylamino-3-aryl-6-(1*H*-1,2,4-triazol-1-yl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones

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Abstract

The carbodiimides **4**, obtained from an aza-Wittig reactions of iminophosphorane **3** with aromatic isocyanates, reacted with primary amines in the presence of catalytic amounts of sodium alkoxide to give selectively 2-alkylamino-3-aryl-6-(1*H*-1,2,4-triazol-1-yl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones **6** in good yields. Compounds **6** exhibit fungicidal activity; e.g., compound **6h** showing the best inhibitive activity (92%) against *Colletotrichum gossypii* in 50 mg/L.

Keywords: Thieno[2,3-*d*]pyrimidin-4(3*H*)-one, 1,2,4-triazole, fungicidal activity, aza-Wittig reaction, isocyanate

Introduction

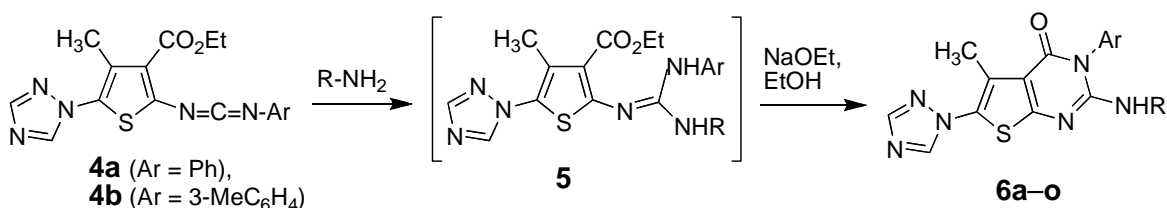
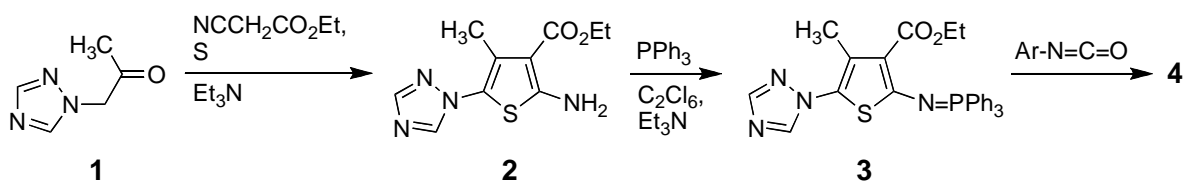
The derivatives of thienopyrimidinone are valued not only for their rich and varied chemistry, but also for many important biological properties. They proved to show significant antifungal, antibacterial, antimalarial and antiallergic activities.¹⁻⁶ The chemistry of thienopyrimidinones have also received attention because their starting materials, 2-amino-3-carboxythiophenes, can conveniently be synthesized by Gewald reaction.⁷ On the other hand, many 1-substituted 1,2,4-triazole compounds show good fungicidal and plant growth regulative activities.^{8,9} The introduction of 1,2,4-triazole to the thienopyrimidine system is expected to influence the biological activities significantly. However, there are few reports about the 1,2,4-triazole substituted thienopyrimidinone system, which is considerable interest as potential agricultural or pharmaceutical fungicides.

The aza-Wittig reactions of iminophosphoranes have received increased attention in view of their utility in the synthesis of nitrogen heterocyclic compounds under mild condition.¹⁰⁻¹⁵ Recently we have been interested in the synthesis of quinazolinones, thienopyrimidinones and

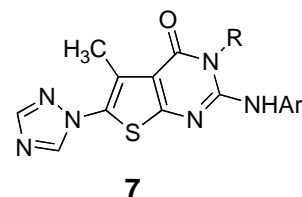
imidazolinones *via* aza-Wittig reaction, with the aim of evaluating their fungicidal activities.¹⁶⁻²² Herein we wish to report a selective synthesis and fungicidal activities of 2-alkylamino-3-aryl-6-(1*H*-1,2,4-triazol-1-yl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones *via* an iminophosphorane **3**.

Results and Discussion

The ethyl 2-amino-4-methyl-5-(1*H*-1,2,4-triazol-1-yl)thiophene-3-carboxylate **2** was obtained by Gewald method from 1-(1*H*-1,2,4-triazol-1-yl)acetone **1**, ethyl cyanoacetate and sulfur in the presence of triethylamine. Compound **2** was easily converted to iminophosphorane **3** by treatment with triphenylphosphine, hexachloroethane and triethylamine in dry acetonitrile in good yield (Scheme 1).



5-7	Ar	R	5-7	Ar	R
a	Ph	Et	i	Ph	<i>c</i> -C ₆ H ₁₂
b	Ph	Pr	j	Ph	PhCH ₂
c	Ph	<i>i</i> -Pr	k	Ph	CH ₂ CH ₂ OH
d	Ph	<i>i</i> -Bu	l	3-MeC ₆ H ₄	Et
e	Ph	<i>t</i> -Bu	m	3-MeC ₆ H ₄	Pr
f	Ph	C ₅ H ₁₁	n	3-MeC ₆ H ₄	Bu
g	Ph	C ₆ H ₁₃	o	3-MeC ₆ H ₄	<i>i</i> -Pr
h	Ph	C ₇ H ₁₅			



Scheme 1

Iminophosphorane **3** reacted with aromatic isocyanates at 0–5 °C to form carbodiimides **4**, which, in turn, reacted with primary amines. In the presence of a catalytic amount of sodium ethoxide at room temperature the presumed guanidine intermediates **5** gave 2-alkylamino-3-aryl-6-(1*H*-1,2,4-triazol-1-yl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (**6a-o**) in good yields (Scheme 1). Isomer **7** was not formed as evidenced by ¹H NMR analysis of the reaction mixture. The structure of **6** was deduced from ¹H NMR data; for example, the ¹H NMR spectrum in **6b** (R = Pr) shows a broad signal at δ 4.26 for NH and a multiplet at δ 3.38–3.33 for NCH₂ of the

NHCH₂CH₂CH₃ group in **6b**. Upon treatment of the sample with D₂O, the ¹H NMR signal of NCH₂ in **6b** collapsed to a triplet at δ 3.35. This result of the deuterium exchange experiment is consistent with structure **6** for the product excluding structure **7**. The formation of **6** can be rationalized by a base catalyzed cyclization of the guanidine intermediate **5** by the more acidic arylamino group to give **6**. The same selectivity has been observed in similar cases.^{22–25}

The investigation of biological activities of **6** showed moderate to good fungicidal activities, 30–92% inhibition activity against *Fusarium oxysporium*, *Rhizoctonia solani*, *Botrytis cinereapers*, *Gibberella zeae*, *Dothiorella gregaria* and *Colletotrichum gossypii* at a dosage of 50 mg/L (Table 2). Compound **6h** showed the best inhibition activities (92%) against *Colletotrichum gossypii* in 50 mg/L. Compared with our previous results on fungicidal activities of some thieno[2,3-*d*]pyrimidin-4(3*H*)-ones, in most cases the attachment of the triazole group to the thienopyrimidinone ring gave better results on fungicidal activities. For example, some 2-substituted 3,5,6,8-tetrahydro-4*H*-thiopyrano[4',3':4,5]thieno[2,3-*d*]pyrimidin-4-ones showed only 9–32% inhibition activities against *Colletotrichum gossypii* in 100 mg/L.²⁶

Table 2. The fungicidal activities of compounds **6**

6	Inhibition rate (% , 50 mg/L)					
	<i>Fusarium oxysporium</i>	<i>Rhizoctonia solani</i>	<i>Botrytis cinereapers</i>	<i>Gibberella zeae</i>	<i>Dothiorella gregaria</i>	<i>Colletotrichum gossypii</i>
a	59	64	44	65	66	52
b	68	74	54	60	46	56
c	90	34	59	52	54	56
d	68	61	40	52	50	65
e	54	61	44	47	62	60
f	59	51	44	52	34	56
g	63	42	54	65	38	87
h	82	92	68	60	86	82
i	49	30	59	34	30	30
j	59	30	35	43	34	45
k	59	45	35	43	38	43
l	38	42	59	60	54	91
m	68	61	44	47	30	52
n	59	45	59	34	30	47
o	49	47	54	34	30	52

In conclusion, we developed a selective synthesis of 2-alkylamino-3-aryl-6-(1*H*-1,2,4-triazol-1-yl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones in good yield via an aza-Wittig reaction. The preliminary investigation of biological activities of **6** shows some good fungicidal activities.

Experimental Section

General Procedures. Melting points were determined using a X-4 model apparatus (Beijing Taike Company). IR were recorded on a PE-983 infrared spectrometer. MS were measured on a Finnigan Trace MS spectrometer (70 eV). NMR were recorded on Varian Mercury 400 and 600 spectrometers. Elementary analyses were taken on a Vario EL III elementary analysis instrument in the Center of Analysis and Testing, College of Chemistry, Central China Normal University.

Ethyl 2-amino-4-methyl-5-(1*H*-1,2,4-triazol-1-yl)thiophene-3-carboxylate (2). To a stirred mixture of 1-(1*H*-1,2,4-triazol-1-yl)acetone **1**²⁷ (0.62 g, 5 mmol), sulfur (0.16 g, 5 mmol), and ethyl cyanoacetate (0.57 g, 5 mmol) in DMF (10 mL) was added triethyl amine (1.2 mL). The mixture was stirred at room temperature for 12 h and poured in water (50 mL); the solid formed was filtered off and recrystallized from ethanol/petroleum ether (1:1) to give light yellow needles **2** (0.67 g, 53%); mp 122–124 °C. ¹H NMR (CDCl₃, 400 MHz): δ 8.24 (s, 1H, triazolyl-3-H), 8.08 (s, 1H, triazolyl-5-H), 6.60 (br, 2H, NH₂), 4.31 (q, 2H, *J* = 7.2 Hz, OCH₂), 2.13 (s, 3H, CH₃), 1.36 (t, *J* = 7.2 Hz, 3H, CH₃). MS: *m/z* (%) 252 (100 M⁺), 224 (11), 206 (81), 178 (51), 124 (17). Anal. calcd. for C₁₀H₁₂N₄O₂S: C, 47.61; H, 4.79; N, 22.21. Found: C, 47.85; H, 4.71; N, 22.05.

***N*-[2-Ethoxycarbonyl-4-methyl-5-(1*H*-1,2,4-triazol-1-yl)thiophene-2-yl]iminotriphenylphosphorane (3).** To a mixture of **2** (2.02 g, 8 mmol), triphenylphosphine (3.14 g, 12 mmol), and hexachloroethane (2.84 g, 12 mmol) in dry acetonitrile (40 mL) was added dropwise triethylamine (2.42 g, 24 mmol) at room temperature. The reaction mixture quickly turned yellow and was stirred for 4 h; the solvent was removed under reduced pressure, and the residue was recrystallized from ethanol to give iminophosphorane **3** (3.32 g, 81%) as light yellow needles; mp 179–181 °C. ¹H NMR (CDCl₃, 400 MHz): δ 8.10–7.48 (m, 17H, Ar-H), 4.35 (q, 2H, *J* = 7.2 Hz, OCH₂), 2.13 (s, 3H, CH₃), 1.38 (t, *J* = 7.2 Hz, 3H, CH₃). MS: *m/z* (%) 512 (100, M⁺), 467 (6), 320 (9), 261 (86), 182 (54), 107 (24). Anal. calcd. for C₂₈H₂₅N₄O₂PS: C, 65.61; H, 4.92; N, 10.93. Found: C, 65.87; H, 4.68; N, 10.97.

2-Alkylamino-3-aryl-6-(1*H*-1,2,4-triazol-1-yl)-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (6a–o). To a solution of iminophosphorane **3** (1.02 g, 2 mmol) in anhydrous dichloromethane (10 mL) was added an phenyl- or 3-methylphenyl isocyanate (2 mmol) under a nitrogen atmosphere at room temperature. The reaction mixture was left at 0–5 °C for 6–12 h when the iminophosphorane **3** had disappeared (as monitored by TLC). The solvent was removed under reduced pressure, diethyl ether/petroleum ether (1:2, 20 mL) was added to precipitate triphenylphosphine oxide. Removal of the solvent gave carbodiimides **4**, which were used without further purification. The appropriate primary alkylamine (2 mmol) was added to the solution of **4** in dichloromethane (15 mL). The reaction mixture was left for 0.5–6 h, the solution was condensed, and anhydrous ethanol (8 mL) with sodium ethoxide (0.2 mmol, 10% equiv) in ethanol was added. The mixture was stirred at room temperature; after 4–6 h the solution was condensed and the residue was recrystallized from ethanol to give **6a–o**.

Ethyl 4-methyl-2-((phenylimino)methyleneamino)-5-(1*H*-1,2,4-triazol-1-yl)thiophene-3-carboxylate (4a) was isolated from the reaction mixture by column chromatography on silica gel as light yellow solid; mp 82–84 °C. IR (KBr): 2253, 1701, 1656, 1530, 1438, 1190 cm⁻¹. ¹H NMR (CDCl₃, 600 MHz): δ 8.23 (s, 1H, triazolyl-3-H), 8.10 (s, 1H, triazolyl-5-H), 7.40–7.21 (m, 5H, Ar-H), 4.33 (q, 2H, *J* = 7.2 Hz, OCH₂), 2.10 (s, 3H, CH₃), 1.37 (t, *J* = 7.2 Hz, 3H, CH₃). MS: *m/z* (%) 353 (M⁺, 100), 307 (62), 293 (34), 265 (74), 178 (67), 124 (47). Anal. calcd. for C₁₇H₁₅N₅O₂S: C, 57.78; H, 4.28; N, 19.82. Found: C, 57.54; H, 4.01; N, 19.95.

2-Ethylamino-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6a). White solid (0.58 g, 83%); mp 164–166 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.33 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.64–7.30 (m, 5H, Ar-H), 4.25 (s, 1H, NH), 3.47–3.40 (m, 2H, NCH₂), 2.39 (s, 3H, CH₃), 1.13 (t, *J* = 7.2 Hz, 3H, CH₃). MS: *m/z* (%) 352 (100, M⁺), 324 (10), 297 (6), 176 (9), 146 (18), 119 (26). Anal. calcd. for C₁₇H₁₆N₆OS (352.4): C, 57.94; H, 4.58; N, 23.85. Found: C, 57.78, H, 4.50; N, 23.97.

5-Methyl-3-phenyl-2-propylamino-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6b). White solid (0.61 g, 84%); mp 166–167 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.63–7.31 (m, 5H, Ar-H), 4.26 (s, 1H, NH), 3.38–3.33 (m, 2H, NCH₂), 2.39 (s, 3H, CH₃), 1.55–1.50 (m, 2H, CH₂), 0.86 (t, *J* = 6.8 Hz, 3H, CH₃). MS: *m/z* (%) 366 (100, M⁺), 323 (15), 311 (21), 296 (14), 269 (17), 118 (23). Anal. calcd. for C₁₈H₁₈N₆OS (366.4): C, 59.00; H, 4.95; N, 22.93. Found: C, 59.24, H, 4.82; N, 23.07.

5-Methyl-3-phenyl-2-isopropylamino-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6c). White solid (0.64 g, 88%); mp 199–201 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.13 (s, 1H, triazolyl-5-H), 7.63–7.29 (m, 5H, Ar-H), 4.28–4.18 (m, 1H, NCH), 4.01 (d, *J* = 6.4 Hz, 1H, NH), 2.39 (s, 3H, CH₃), 1.13 (d, *J* = 6.8 Hz, 6H, 2CH₃). MS: *m/z* (%) 366 (100, M⁺), 350 (5), 338 (15), 323 (10), 311 (36), 296 (24), 269 (27), 118 (22). Anal. calcd. for C₁₈H₁₈N₆OS (366.4): C, 59.00; H, 4.95; N, 22.93. Found: C, 58.83, H, 4.98; N, 22.71.

2-Isobutylamino-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6d). White solid (yield 0.61 g, 80%), mp 167–169 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.65–7.31 (m, 5H, Ar-H), 4.28 (t, *J* = 5.2 Hz, 1H, NH), 3.22 (t, *J* = 6.4 Hz, 2H, NCH₂), 2.39 (s, 3H, CH₃), 1.81–1.69 (m, 1H, CH), 0.83 (d, *J* = 6.8 Hz, 6H, 2CH₃). MS: *m/z* (%) 380 (100, M⁺), 337 (11), 324 (67), 296 (47), 269 (45), 206 (11), 176 (11), 118 (19). Anal. calcd. for C₁₉H₂₀N₆OS (380.5): C, 59.98; H, 5.30; N, 22.09. Found: C, 59.93, H, 5.14; N, 22.35.

2-(*tert*-Butylamino)-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6e). White solid (yield 0.59 g, 78%), mp 168–170 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.62–7.28 (m, 5H, Ar-H), 4.12 (s, 1H, NH), 1.36 (s, 9H, 3CH₃). MS: *m/z* (%) 380 (100, M⁺), 324 (56), 296 (47), 269 (36), 178 (6), 118 (21). Anal. calcd. for C₁₉H₂₀N₆OS (380.5): C, 59.98; H, 5.30; N, 22.09. Found: C, 60.17, H, 5.10; N, 22.15.

5-Methyl-2-pentylamino-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6f). White solid (0.64 g, 81%), mp 150–152 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H,

triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.65–7.30 (m, 5H, Ar-H), 4.23 (s, 1H, NH), 3.40–3.35 (m, 2H, NCH₂), 2.39 (s, 3H, CH₃), 1.64–1.19 (m, 6H, 3CH₂), 0.87 (t, *J* = 7.2 Hz, 3H, CH₃). MS: *m/z* (%) 394 (100, M⁺), 366 (12), 339 (10), 323 (16), 270 (17), 177 (13), 117 (32). Anal. calcd. for C₂₀H₂₂N₆OS (394.5): C, 60.89; H, 5.62; N, 21.30. Found: C, 60.64, H, 5.72; N, 21.17.

2-Hexylamino-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6g). White solid (0.60 g, 74%), mp 142–144 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.11 (s, 1H, triazolyl-5-H), 7.64–7.30 (m, 5H, Ar-H), 4.25 (s, 1H, NH), 3.40–3.35 (m, 2H, NCH₂), 2.39 (s, 3H, CH₃), 1.48–1.24 (m, 8H, 4CH₂), 0.86 (t, *J* = 7.2 Hz, 3H, CH₃). MS: *m/z* (%) 408 (100, M⁺), 353 (10), 337 (10), 323 (17), 308 (18), 296 (28), 270 (17), 117 (27), 91 (16). Anal. calcd. for C₂₁H₂₄N₆OS (408.5): C, 61.74; H, 5.92; N, 20.57. Found: C, 60.81, H, 5.98; N, 20.44.

2-Heptylamino-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6h). White solid (0.61 g, 72%), mp 105–107 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.65–7.30 (m, 5H, Ar-H), 4.23 (s, 1H, NH), 3.40–3.35 (m, 2H, NCH₂), 2.39 (s, 3H, CH₃), 1.50–1.24 (m, 10H, 5CH₂), 0.87 (t, *J* = 6.8 Hz, 3H, CH₃). MS: *m/z* (%) 422 (100, M⁺), 394 (16), 379 (14), 351 (16), 337 (20), 323 (48), 296 (37), 270 (27), 118 (45), 90 (27). Anal. calcd. for C₂₂H₂₆N₆OS (422.6): C, 62.53; H, 6.20; N, 19.89. Found: C, 62.71, H, 6.36; N, 19.74.

2-Cyclohexylamino-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6i). White solid (0.71 g, 87%); mp 208–210 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.13 (s, 1H, triazolyl-5-H), 7.64–7.29 (m, 5H, Ar-H), 4.08 (d, *J* = 7.6 Hz, 1H, NH), 3.98–3.88 (m, 1H, NCH), 2.39 (s, 3H, CH₃), 1.94–1.03 (m, 10H, 5CH₂). MS: *m/z* (%) 406 (100, M⁺), 380 (25), 352 (10), 324 (89), 296 (48), 269 (47), 205 (10), 118 (37). Anal. calcd. for C₂₁H₂₂N₆OS (406.5): C, 62.05; H, 5.45; N, 20.67. Found: C, 62.31, H, 5.37; N, 20.58.

5-Methyl-3-phenyl-2-phenylmethylamino-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6j). White solid (0.74 g, 89%), mp 157–159 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.32 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.61–7.20 (m, 10H, Ar-H), 4.66–4.60 (m, 3H, NH and CH₂), 2.40 (s, 3H, CH₃). MS: *m/z* (%) 414 (100, M⁺), 359 (8), 322 (8), 269 (9), 181 (12), 167 (27), 149 (24), 118 (10). Anal. calcd. for C₂₂H₁₈N₆OS (414.5): C, 63.75; H, 4.38; N, 20.28. Found: C, 63.61, H, 4.35; N, 20.47.

2-(2-Hydroxyethylamino)-5-methyl-3-phenyl-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6k). White solid (0.60 g, 82%), mp 172–174 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.33 (s, 1H, triazolyl-3-H), 8.12 (s, 1H, triazolyl-5-H), 7.65–7.32 (m, 5H, Ar-H), 4.75 (s, 1H, NH), 4.18 (s, 1H, OH), 3.78–3.72 (m, 2H, OCH₂), 3.60–3.55 (m, 2H, NCH₂), 2.40 (s, 3H, CH₃). MS: *m/z* (%) 368 (100, M⁺), 340 (6), 323 (20), 313 (8), 295 (13), 269 (15), 178 (3), 119 (9). Anal. calcd. for C₁₇H₁₆N₆OS (368.4): C, 55.42; H, 4.38; N, 22.81. Found: C, 55.34, H, 4.39; N, 22.64.

2-(Ethylamino)-5-methyl-3-(3-methylphenyl)-6-(1*H*-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (6l). White solid (0.63 g, 86%), mp 204–206 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.34 (s, 1H, triazolyl-3-H), 8.13 (s, 1H, triazolyl-5-H), 7.53–7.09 (m, 4H, Ar-H), 4.30 (s, 1H, NH), 3.46–3.41 (m, 2H, NCH₂), 2.45 (s, 3H, CH₃), 2.39 (s, 3H, CH₃), 1.14 (t, *J* = 7.2 Hz, 3H, CH₃).

MS: m/z (%) 366 (46, M^+), 338 (9), 311 (25), 206 (9), 132 (52), 91 (100). Anal. calcd. for $C_{18}H_{18}N_6OS$ (366.4): C, 59.00; H, 4.95; N, 22.93. Found: C, 59.17, H, 5.18; N, 22.68.

5-Methyl-3-(3-methylphenyl)-2-propylamino-6-(1H-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3H)-one (6m). White solid (0.67 g, 88%), mp 212–214 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H, triazolyl-3-H), 8.13 (s, 1H, triazolyl-5-H), 7.53–7.10 (m, 4H, Ar-H), 4.33 (s, 1H, NH), 3.39–3.31 (m, 2H, NCH_2), 2.45 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.56–1.51 (m, 2H, CH_2), 0.86 (d, $J = 7.2$ Hz, 3H, CH_3). MS: m/z (%) 380 (100, M^+), 352 (17), 338 (21), 325 (18), 310 (20), 282 (18), 132 (16), 91 (30). Anal. calcd. for $C_{19}H_{20}N_6OS$ (380.5): C, 59.98; H, 5.30; N, 22.09. Found: C, 59.76, H, 5.38; N, 22.13.

2-Butylamino-5-methyl-3-(3-methylphenyl)-6-(1H-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3H)-one (6n). White solid (0.67 g, 85%), mp 188–190 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H, triazolyl-3-H), 8.13 (s, 1H, triazolyl-5-H), 7.52–7.09 (m, 4H, Ar-H), 4.28 (s, 1H, NH), 3.40–3.36 (m, 2H, NCH_2), 2.44 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.50–1.25 (m, 4H, $2CH_2$), 0.90 (t, $J = 7.2$ Hz, 3H, CH_3). MS: m/z (%) 394 (93, M^+), 380 (13), 340 (14), 310 (26), 283 (40), 132 (94), 91 (100). Anal. calcd. for $C_{20}H_{22}N_6OS$ (394.5): C, 60.89; H, 5.62; N, 21.30. Found: C, 60.96, H, 5.44; N, 21.48.

5-Methyl-3-(3-methylphenyl)-2-isopropylamino-6-(1H-1,2,4-triazol-1-yl)thieno[2,3-*d*]pyrimidin-4(3H)-one (6o). White solid (0.60 g, 79%), mp 209–211 °C. 1H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H, triazolyl-3-H), 8.13 (s, 1H, triazolyl-5-H), 7.53–7.08 (m, 4H, Ar-H), 4.25–4.18 (m, 1H, NCH), 4.06 (d, $J = 8.0$ Hz, 1H, NH), 2.45 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.14 (d, $J = 6.8$ Hz, 6H, $2CH_3$). MS: m/z (%) 380 (16, M^+), 325 (9), 283 (27), 133 (100), 91 (76). Anal. calcd. for $C_{19}H_{20}N_6OS$ (380.5): C, 59.98; H, 5.30; N, 22.09. Found: C, 59.88, H, 5.14; N, 22.15.

Bioassays of fungicidal activities

The samples were dissolved in DMF (10 mL) at a concentration of 500 mg/L. The solutions (1 mL) were rapidly mixed with thawed potato glucose agar culture medium (9 mL) below 50 °C. The mixture was poured on Petri dishes and cooled. The solidified plates were incubated with 4 mm mycelium disk, inverted, and incubated at 28 °C for 48 h. The mixed medium without sample was used as the blank control. The mycelia elongation radius (mm) of fungi settlements was measured after 48 h of culture. The growth inhibition rates were calculated with the following equation: $I = [(C-T)/C] \times 100\%$ [I is the growth inhibition rate (%), C is the control settlement radius (mm), and T is the treatment group fungi settlement radius (mm)].

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