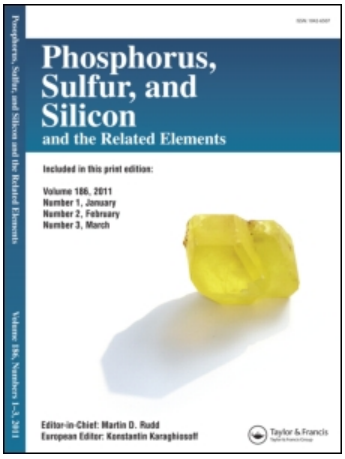

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Efficient Synthesis and Fungicidal Activities of 2-Alkylthiobenzofuro[3,2-*d*]Pyrimidinones

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EFFICIENT SYNTHESIS AND FUNGICIDAL ACTIVITIES OF 2-ALKYLTHIOBENZOFURO[3,2-*d*]PYRIMIDINONES

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2-Alkylthiobenzofuro[3,2-d]pyrimidinones 5 and 6 were synthesized by S-alkylation of 2,3-dihydro-2-thioxobenzofuro[3,2-d]pyrimidin-4(1H)-ones 4, which were obtained via aza-Wittig reaction of iminophosphorane 2 with CS_2 and further reaction of the product with various amines. Compounds 5 and 6 exhibited fungicidal activity. For example, compound 6a, which has a small N-substituted methyl group, showed the best inhibitive activity (91%) against* Dothiorella gregaria *at 50 mg/L.

Supplemental materials are available for this article. Go to the publisher's online edition of* Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.

Keywords Aza-Wittig reaction; benzofuro[3,2-*d*]pyrimidinone; carbon disulfide; fungicidal activity; iminophosphorane

INTRODUCTION

The derivatives of heterocycles containing the benzofuropyrimidinone system are of great importance because of their remarkable biological properties. For example, some derivatives of benzofuropyrimidinones have shown good analgesic, anti-inflammatory, and antimicrobial activities,[1,2] whereas others exhibited good anticoccidial and blood sugar-lowering activities.[3,4] The literature-reported methods for the preparation of some representative derivatives of benzofuro[3,2-*d*]pyrimidin-4(3*H*)-one involve the reaction of 3-amino-2-(ethoxycarbonyl) benzofuran with orthoformate and an amine, the rearrangement of benzofuro[3,2-*d*]oxazines by treatment with an amine, or the cyclization of 3-amino-2-(aminocarbonyl)benzofuran with acyl chlorides.[5–8] However, 2-thioxobenzofuro[3,2-*d*]pyrimidin-4(3*H*)-ones are not easily accessible by currently existing routes. Recently aza-Wittig reactions were applied to produce carbodiimides able to undergo a plethora of

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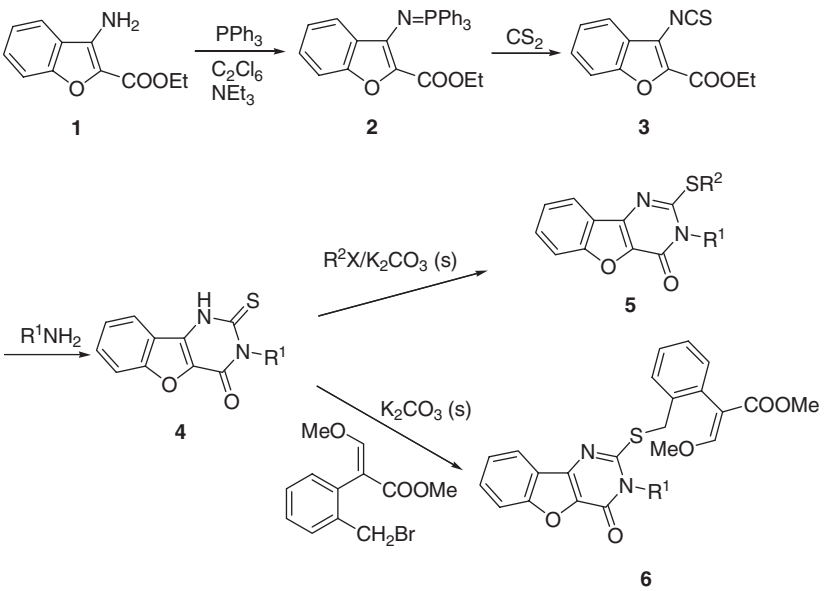
heterocyclization reactions.[9–12] We have been interested in the synthesis of quinazolinones, thienopyrimidinones, and imidazolinones via the reaction of α- or β-ethoxycarbonyl carbodiimides with various nucleophiles under mild conditions.[13–18] The method was also utilized in the synthesis of some 2-amino or 2-aryl(alkyl)oxy substituted benzofuro[3,2-*d*]pyrimidin-4(3*H*)-ones.[16] In this article we wish to report further an efficient synthesis and fungicidal activities of 2-alkylthio substituted benzofuro[3,2-*d*]pyrimidin-4(3*H*)-ones by the aza-Wittig reaction of β-ethoxycarbonyl iminophosphorane **2** with CS_2, followed by reaction with amines and halides under basic conditions.

RESULTS AND DISCUSSION

As shown in Scheme 1, iminophosphorane **2**, obtained from amine **1** with triphenylphosphine, hexachloroethane, and triethylamine, reacted with excess carbon disulfide to give isothiocyanate **3**. While the reaction of **3** with aliphatic primary amines took place smoothly at room temperature to give directly 2-thioxobenzofuro[3,2-d]pyrimidin-4(1*H*)-one **4** in 72–88% yields, aromatic primary amines required reaction in acetonitrile in the presence of sodium ethoxide. The results are listed in Table I. S-Alkylation of **4** with alkyl halides or methyl 3-(2-(bromomethyl)phenyl)-3-methoxyacrylate in the presence of potassium carbonate provided 2-alkylthio-benzofuro[3,2-*d*]pyrimidin-4(3*H*)-ones **6** and **7** in 74–89% yields at 50°C. There are no obvious effects of the R^1 or R^2 groups on the reaction, and the products **6** and **7** were obtained in good yields. It is noteworthy that isothiocyante **3** can generally be prepared from the reaction of the corresponding ethyl 3-aminobenzofuran-2-carboxylate with the highly toxic thiophosgene. The method described here provides an efficient synthesis of isothiocyante **3** without using the highly toxic thiophosgene. The methyl 3-(2-(bromomethyl)phenyl)-3-methoxyacrylate was selected as the main halide because the products **6** obtained can be regarded as the analogues of



Scheme 1

Table I Preparation of compounds **4**, **5**, and **6**

Compd.	R^1	R^2X	Condition	Yield (%)
4a	Me		r.t. / 05 h	84
4b	Et		r.t. / 0.5 h	86
4c	*n*-Pr		r.t. / 1 h	82
4d	*n*-Bu		r.t. / 1 h	81
4e	*n*-C_5H_{11}		r.t. / 1 h	72
4f	$PhCH_2$		r.t. / 1 h	86
4g	H		r.t. / 0.5 h	88
4h	4-ClC_6H_4		r.t. / 3 h[a]	80
5a	*n*-Pr	*n*-PrBr	50 °C / 3 h	86
5b	*n*-Pr	$PhCH_2Cl$	50 °C / 4 h	82
5c	*n*-Pr	*n*-BuBr	50 °C / 4 h	85
5d	*n*-Pr	$BrCH_2COOEt$	50 °C / 2 h	86
6a	Me		50 °C / 4 h	87
6b	Et		50 °C / 4 h	88
6c	*n*-Pr		50 °C / 6 h	87
6d	*n*-Bu		50 °C / 5 h	79
6e	*n*-C_5H_{11}		50 °C / 5 h	74
6f	$PhCH_2$		50 °C / 4 h	86
6g	H		50 °C / 4 h	89
6h	4-ClC_6H_4		50 °C / 6 h	84

[a]Then treated with sodium ethoxide in ethanol at r.t. for 2 h.

Strobilurin fungicides. Strobilurin fungicides are an important class of agricultural fungicides and exhibit strong fungicidal activity against various fungi by binding to electron transfer at the ubiquinol-oxidation center (Qo-site) of the bc1-enzyme complex (complex III).[19–21] By using the above synthetic method, the new Strobilurin derivatives **6** containing benzofuro[3,2-*d*]pyrimidinone were obtained in good yields.

The structure of compounds **5** and **6** was confirmed by their spectral data. For example, the ^{1}H NMR spectrum of **6b** shows two singlets at 3.72 and 3.86 ppm and a singlet due to the two OCH_3, respectively. The signals of NCH_2CH_3 appear at 1.36 ppm as triplets and 4.24 ppm as quarterlets, respectively. The signals attributable to the Ar–Hs are found at 7.18–8.05 ppm as multiplet respectively. The IR spectra of **6b** revealed C=O absorption bands at 1700 cm^{-1}. The MS spectrum of **6b** shows a molecular ion peak at *m/z* 450 with 11% abundance.

The biological activities of **5** and **6** were investigated (see the Supplemental Materials available online, Table S1).

In conclusion, we described an efficient synthesis of 2-alkylthio substituted benzofuro[3,2-*d*]pyrimidin-4(3*H*)-ones by the aza-Wittig reaction. This protocol presented many advantages, such as good to excellent yields, mild reaction conditions, readily available starting materials, and simple purification procedure. The preliminary investigation on the biological activities shows that one of the compounds exhibited good fungicidal activities.

EXPERIMENTAL

Unless otherwise noted, all materials were commercially available and were used directly without further purification. All solvents were redistilled before use. ^{1}H NMR

spectra were recorded on a Mercury-Plus 400 or 600 spectrometer in $CDCl_3$ or DMSO-d_6 with TMS as the internal reference. MS spectra were determined using a Trace MS 2000 organic mass spectrometer. Elemental analyses were performed on a Vario EL III elemental analysis instrument. Melting points were taken on an X-4 binocular microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and are uncorrected. The iminophosphorane **2** was prepared according to the reported method.[12]

General Preparation of 2,3-Dihydro-2-thioxobenzofuro [3,2-d]pyrimidin-4(1*H*)-one 4a-4h

To a solution of iminophosphorane **2** (9.30 g, 20 mmol) in anhydrous methylene dichloride and acetonitrile (20 mL, v/v = 1:1), excess carbon disulfide (15 mL) was added. After the reaction mixture was refluxed for 24–28 h, the solvent was condensed under reduced pressure and ether (10 mL) was added to precipitate triphenylphosphine sulfide. The precipitate was removed by filtration, and the filtrate was evaporated to give ethyl 3-isothiocyanato-benzofuran-2-carboxylate **3**, which was used directly without further purification. To a solution of the crude **3** in CH_3CN (20 mL), amine (20 mmol) was added and the mixture was stirred for 0.5–1 h at room temperature. While an aromatic amine was used, the solvent was removed, and anhydrous EtOH (10 mL) with several drops of EtONa in EtOH was added. The mixture was stirred for 2 h at room temperature. The precipitated solid was collected and washed with ethanol and crystallized from methylene dichloride/petroleum ether to give 2,3-dihydro-2-thioxobenzofuro[3,2-d]pyrimidin-4(1*H*)-ones **4**.

3-Methyl-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1*H*)-one (4a). White solid, mp > 300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 3.70 (s, 3H, NCH_3), 7.36–7.95 (m, 4H, Ar—H). MS (70 eV) m/z (%): 232 (M^+, 100), 202 (7), 159 (30), 130 (10), 103 (33), 76 (5). Anal. Calcd for $C_{11}H_8N_2O_2S$ (232.3): C, 56.88; H, 3.47; N, 12.06. Found: C, 56.71, H, 3.69; N, 12.24.

3-Ethyl-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4b). White solid, mp > 300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 1.17 (t, J = 7.2 Hz, 3H, CH_3), 4.59 (q, J = 7.2 Hz, 2H, NCH_2), 7.38–7.96 (m, 4H, Ar—H). MS (70 eV) m/z (%): 246 (M^+, 100), 218 (56), 202 (34), 159 (55), 130 (26), 103 (58), 77 (40). Anal. Calcd for $C_{12}H_{10}N_2O_2S$ (246.3): C, 58.52; H, 4.09; N, 11.37. Found: C, 58.27, H, 4.04; N, 11.48.

3-Propyl-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4c). White solid, mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 0.89 (t, J = 7.2 Hz, 3H, CH_3), 1.52–1.58 (m, 2H, CH_2), 4.45 (t, J = 7.2 Hz, 2H, NCH_2), 7.35–7.93 (m, 4H, Ar—H). MS (70 eV) m/z (%): 260 (M^+, 66), 217 (98), 158 (100), 129 (31), 102 (82), 76 (16). Anal. Calcd for $C_{13}H_{12}N_2O_2S$ (260.3): C, 59.98; H, 4.65; N, 10.76. Found: C, 59.84, H, 4.46; N, 10.84.

3-Butyl-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4d). White solid, mp 295–296 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 0.93 (t, J = 7.2 Hz, 3H, CH_3), 1.40–1.78 (m, 4H, 2×CH_2), 4.17 (t, J = 7.2 Hz, 2H, NCH_2), 7.36–7.98 (m, 4H, Ar—H). MS (70 eV) m/z (%): 274 (M^+, 59), 241 (100), 218 (35), 202 (36), 160 (33), 130 (11), 103 (30), 76 (7). Anal. Calcd for $C_{14}H_{14}N_2O_2S$ (274.3): C, 61.29; H, 5.14; N, 10.21. Found: C, 61.48, H, 5.12; N, 10.07.

3-Pentyl-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4e). White solid, mp 290–292 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 0.82 (t, J = 7.2 Hz, 3H, CH_3), 1.24–2.87 (m, 6H, 3×CH_2), 4.50 (t, J = 7.2 Hz, 2H, CH_2), 7.36–7.94 (m, 4H,

Ar—H). MS (70 eV) m/z (%): 288 (M^+, 16), 255 (100), 217 (39), 201 (31), 158 (35), 129 (11), 102 (43), 87 (20). Anal. Calcd for $C_{15}H_{16}N_2O_2S$ (288.4): C, 62.48; H, 5.59; N, 9.71. Found: C, 62.54, H, 5.32; N, 9.53.

3-Benzyl-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4f). White solid, mp > 300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 5.86 (s, 2H, CH_2), 7.17–7.94 (m, 9H, Ar—H), 8.07 (s, 1H, NH). MS (70 eV) m/z (%): 308 (100), 275 (43), 202 (6), 148 (4), 91 (8). Anal. Calcd for $C_{17}H_{12}N_2O_2S$ (308.4): C, 66.22; H, 3.92; N, 9.08. Found: C, 66.14, H, 3.75; N, 9.26.

2-Thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4g). White solid, mp > 300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 7.36–7.65 (m, 3H, Ar—H), 7.92–7.93 (m, 1H, Ar—H). MS (70 eV) m/z (%): 218 (M^+, 77), 160 (41), 103 (100), 76 (28). Anal. Calcd for $C_{10}H_6N_2O_2S$ (218.2): C, 55.04; H, 2.77; N, 12.84. Found: C, 55.19, H, 2.64; N, 12.95.

3-(4-Chlorophenyl)-2-thioxo-2,3-dihydrobenzofuro[3,2-d]pyrimidin-4(1H)-one (4h). White solid, mp > 300 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 7.35–8.26 (m, 8H, Ar—H). MS (70 eV) m/z (%): 328 (M^+, 100), 295 (18), 202 (25), 159 (56), 130 (29), 103 (59), 76 (18). Anal. Calcd for $C_{16}H_9ClN_2O_2S$ (328.8): C, 58.45; H, 2.76; N, 8.52. Found: C, 58.22, H, 2.81; N, 8.78.

General Preparation of 2-Alkylthiobenzofuro[3,2-d]pyrimidin-4(3*H*)-one 5a–5d and 6a–6h

To a solution of 2,3-dihydro-2-thioxobenzofuro[3,2-d]pyrimidin-4(1*H*)-one **4** (1 mmol) in dry DMF (5 mL), alkyl halide (1 mmol) and solid potassium carbonate (0.28 g, 2 mmol) were added. The mixture was stirred for 3–6 h at 50 °C. The solution was cooled and diluted with water (20 mL). The solid product obtained was filtered and recrystallized from methylene dichloride/petroleum ether (v/v) to give 2-alkylthiobenzofuro[3,2-d]pyrimidin-4(3*H*)-ones **5** and **6**.

3-Propyl-2-propylthiobenzofuro[3,2-d]pyrimidin-4(3H)-one (5a). White crystals, mp 122–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 1.02 (t, J = 7.2 Hz, 3H, CH_3), 1.10 (t, J = 7.2 Hz, 3H, CH_3), 1.82–1.89 (m, 4H, $2CH_2$), 3.34 (t, J = 7.2 Hz, 2H, SCH_2), 4.18 (t, J = 7.2 Hz, 2H, NCH_2), 7.39–8.01 (m, 4H, Ar—H). ^{13}C NMR (100 MHz, $CDCl_3$): 157.9, 156.8, 153.5, 142.3, 136.1, 129.2, 123.5, 122.3, 121.1, 112.6, 46.1, 34.3, 21.9, 21.1, 13.4, 11.1. MS (70 eV) m/z (%): 302 (M^+, 100), 259 (86), 232 (21), 217 (62), 202 (32), 160 (32), 130 (22), 102 (30). Anal. Calcd for $C_{16}H_{18}N_2O_2S$ (302.4): C, 63.55; H, 6.00; N, 9.26. Found: C, 63.78; H, 5.84; N, 9.49.

2-Benzylthio-3-propylbenzofuro[3,2-d]pyrimidin-4(3H)-one (5b). White crystals, mp 118–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 0.99 (t, J = 7.2 Hz, 3H, CH_3), 1.79–1.85 (m, 2H, CH_2), 4.18 (t, J = 7.2 Hz, 2H, NCH_2), 4.60 (s, 2H, SCH_2), 7.29–8.06 (m, 9H, Ar—H). ^{13}C NMR (100 MHz, $CDCl_3$): 157.0, 156.6, 153.2, 142.0, 136.0, 135.6, 129.1, 129.0, 128.2, 127.3, 123.4, 122.0, 120.9, 112.5, 45.9, 36.6, 20.9, 10.8. MS (70 eV) m/z (%): 350 (M^+, 100), 317 (25), 308 (31), 275 (80), 260 (89), 232 (21), 202 (46), 159 (20), 130 (24), 102 (20), 91 (93). Anal. Calcd for $C_{20}H_{18}N_2O_2S$ (350.4): C, 68.55; H, 5.18; N, 7.99. Found: C, 68.39; H, 5.26; N, 7.88.

2-Butylthio-3-propylbenzofuro[3,2-d]pyrimidin-4(3H)-one (5c). White crystals, mp 130–131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 1.00 (t, J = 7.2 Hz, 3H, CH_3), 1.04 (t, J = 7.2 Hz, 3H, CH_3), 1.52–1.87 (m, 6H, $3CH_2$), 3.36 (t, J = 7.2 Hz, 2H, SCH_2),

4.18 (t, $J = 7.2$ Hz, 2H, NCH_2), 7.40–8.00 (m, 4H, Ar—H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.0, 156.9, 153.6, 142.4, 136.2, 129.3, 123.6, 122.4, 121.2, 112.7, 46.1, 32.1, 30.6, 22.0, 21.1, 13.6, 11.2. MS (70 eV) m/z (%): 316 (M^+, 36), 258 (81), 231 (51), 217 (100), 201 (60), 184 (38), 158 (72), 128 (65), 101 (66). Anal. Calcd for $C_{17}H_{20}N_2O_2S$ (316.4): C, 64.53; H, 6.37; N, 8.85. Found: C, 64.47; H, 6.31; N, 8.76.

Ethyl 2-(3-propylbenzofuro[3,2-d]pyrimidin-4(3H)-on-2-ylthio)acetate (5d). White crystals, mp 142–143 °C. ^1H NMR (400 MHz, $CDCl_3$): 1.04 (t, $J = 7.2$ Hz, 3H, CH_3), 1.29 (t, $J = 7.2$ Hz, 3H, CH_3), 1.86–1.91 (m, 2H, CH_2), 4.08 (s, 2H, SCH_2), 4.17–4.29 (q, $J = 7.2$ Hz, 4H, $2CH_2$), 7.39–7.95 (m, 4H, Ar—H). MS (70 eV) m/z (%): 346 (M^+, 100), 300 (13), 260 (67), 230 (23), 202 (10), 172 (15), 130 (13). Anal. Calcd for $C_{17}H_{18}N_2O_4S$ (346.4): C, 58.94; H, 5.24; N, 8.09. Found: C, 58.77; H, 5.36; N, 8.01.

Methyl (2E)-3-methoxy-2-(2-{[(3-methyl-4-oxo-3,4-dihydrobenzofuro[3,2-d]pyrimidin-2-yl) thio]methyl}phenyl)acrylate (6a). White solid, mp 160–162 °C. ^1H NMR (600 MHz, $CDCl_3$): 3.62 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.58 (s, 2H, SCH_2), 7.17–8.06 (m, 9H, Ar—H and CH=). IR (KBr): 1700 (C=O), 1625, 1516, 1350, 1258 cm^{-1}. MS (70 eV) m/z (%): 436 (M^+, 9), 404 (25), 357 (8), 301 (100), 232 (20), 202 (19), 145 (99), 130 (30), 115 (34), 103 (40), 91 (8). Anal. Calcd for $C_{23}H_{20}N_2O_5S$ (436.5): C, 63.29; H, 4.62; N, 6.42. Found: C, 63.17, H, 4.71; N, 6.19.

Methyl (2E)-3-methoxy-2-(2-{[(3-ethyl-4-oxo-3,4-dihydrobenzofuro[3,2-d]pyrimidin-2-yl)thio] methyl}phenyl)acrylate (6b). White solid, mp 152–154 °C. ^1H NMR (600 MHz, $CDCl_3$): 1.36 (t, $J = 7.2$ Hz, 3H, CH_3), 3.72 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.24 (q, $J = 7.2$ Hz, 2H, NCH_2), 4.56 (s, 2H, SCH_2), 7.18–8.05 (m, 9H, Ar—H and CH=). ^{13}C NMR (100 MHz, $CDCl_3$): 167.8, 160.2, 157.8, 157.0, 153.4, 142.4, 136.3, 135.0, 132.9, 131.4, 130.3, 129.5, 128.2, 127.7, 123.8, 122.4, 121.3, 112.9, 110.2, 62.0, 51.7, 39.9, 35.0, 13.0. IR (KBr): 1700 (C=O), 1518, 1253, 1119 cm^{-1}. MS (70 eV) m/z (%): 450 (M^+, 11), 418 (17), 315 (100), 245 (10), 204 (6), 145 (44), 129 (6), 115 (10), 102 (9). Anal. Calcd for $C_{24}H_{22}N_2O_5S$ (450.5): C, 63.98; H, 4.92; N, 6.22; Found: C, 63.79, H, 5.11; N, 6.03.

Methyl (2E)-3-methoxy-2-(2-{[(3-propyl-4-oxo-3,4-dihydrobenzofuro[3,2-d]pyrimidin-2-yl)thio] methyl}phenyl)acrylate (6c). White solid, mp 148–150 °C. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 0.99$ (t, $J = 7.2$ Hz, 3H, CH_3), 1.77–1.81 (m, 2H, CH_2), 3.72 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.12 (t, $J = 7.2$ Hz, 2H, NCH_2), 4.56 (s, 2H, SCH_2), 7.17–8.04 (m, 9H, Ar—H and CH=). IR (KBr): 1688 (C=O), 1632, 1518, 1253 cm^{-1}. MS (70 eV) m/z (%): 464 (M^+, 12), 432 (17), 329 (100), 287 (9), 259 (27), 204 (38), 145 (90), 129 (41), 115 (35), 103 (40), 91 (10). Anal. Calcd for $C_{25}H_{24}N_2O_5S$ (464.5): C, 64.64; H, 5.21; N, 6.03. Found: C, 64.55; H, 5.32; N, 5.91.

Methyl (2E)-3-methoxy-2-(2-{[(3-butyl-4-oxo-3,4-dihydrobenzofuro[3,2-d]pyrimidin-2-yl)thio] methyl}phenyl)acrylate (6d). White solid, mp 103–105 °C. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.2$ Hz, 3H, CH_3), 1.40–1.75 (m, 4H, CH_2CH_2), 3.72 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.15 (t, $J = 7.2$ Hz, 2H, NCH_2), 4.57 (s, 2H, SCH_2), 7.18–8.04 (m, 9H, Ar—H and CH=). MS (70 eV) m/z (%): 478 (M^+, 6), 445 (7), 343 (100), 287 (8), 273 (10), 218 (11), 202 (15), 186 (8), 145 (32), 115 (7). Anal. Calcd for $C_{26}H_{26}N_2O_5S$ (478.6): C, 65.25; H, 5.48; N, 5.85. Found: C, 65.06; H, 5.36; N, 5.77.

Methyl (2E)-3-methoxy-2-(2-{[(3-pentyl-4-oxo-3,4-dihydrobenzofuro[3,2-d]pyrimidin-2-yl)thio] methyl}phenyl)acrylate (6e). White solid, mp 92–93 °C. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.91$ (t, $J = 7.2$ Hz, 3H, CH_3), 1.36–1.76 (m, 6H, $CH_2CH_2CH_2$), 3.70 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.14 (t, $J = 7.2$ Hz, 2H, NCH_2),

4.57 (s, 2H, SCH_2), 7.17–8.04 (m, 9H, Ar—H and CH=). IR (KBr): 1700 (C=O), 1625, 1516, 1126 cm^{-1}. MS (70 eV) m/z (%): 492 (M^+, 8), 460 (13), 357 (100), 287 (14), 204 (7), 145 (31), 115 (4). Anal. Calcd for $C_{27}H_{28}N_2O_5S$ (492.6): C, 65.83; H, 5.73; N, 5.69; Found: C, 65.89; H, 5.64; N, 5.57.

Methyl (2E)-3-methoxy-2-(2-{[(3-benzyl-4-oxo-3,4-dihydrobenzofuro[3, 2-d]pyrimidin-2-yl)thio] methyl}phenyl)acrylate (6f). White solid, mp 206–207 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.66 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 4.53 (s, 2H, SCH_2), 5.43 (s, 2H, NCH_2), 7.14–8.05 (m, 14H, Ar—H and CH=). ^{13}C NMR (100 MHz, $CDCl_3$): 167.8, 160.3, 158.5, 156.9, 153.7, 142.4, 135.8, 135.1, 132.8, 132.2, 132.1, 131.5, 131.3, 130.2, 129.5, 128.5, 128.3, 128.2, 127.7, 123.8, 122.3, 121.3, 112.8, 110.1, 61.9, 51.6, 35.0, 30.2. IR (KBr): 1702 (C=O), 1633, 1512, 1254, 1130 cm^{-1}. MS (70 eV) m/z (%): 512 (M^+, 9), 480 (12), 389 (15), 377 (100), 307 (54), 275 (37), 248 (15), 202 (42), 145 (80), 130 (26), 115 (17), 103 (12), 91 (38). Anal. Calcd for $C_{29}H_{24}N_2O_5S$ (512.6): C, 67.95; H, 4.72; N, 5.47. Found: C, 68.12; H, 4.68; N, 5.31.

Methyl (2E)-3-methoxy-2-(2-{[(4-oxo-3,4-dihydrobenzofuro[3,2-d]pyrimi din-2-yl)thio]methyl} phenyl)acrylate (6g). White solid, mp 238–240 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.53 (s, 2H, SCH_2), 7.15–8.08 (m, 9H, Ar—H and CH=), 11.57 (s, 1H, NH). MS (70 eV) m/z (%): 422 (M^+, 100), 390 (84), 357 (11), 330 (10), 287 (7), 189 (76), 145 (39), 130 (28), 102 (99), 75 (43). Anal. Calcd for $C_{22}H_{18}N_2O_5S$ (422.4): C, 62.55; H, 4.29; N, 6.63. Found: C, 62.37; H, 4.08; N, 6.45.

Methyl (2E)-3-methoxy-2-(2-[{[3-(4-chlorophenyl)-4-oxo-3,4-dihydroben zofuro[3,2-d] pyrimidin-2-yl]thio}methyl]phenyl)acrylate (6h). White solid, mp 210–212 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 3.60 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 4.43 (s, 2H, SCH_2), 7.10–8.11 (m, 13H, Ar—H and CH=). ^{13}C NMR (100 MHz, $CDCl_3$): 167.7, 160.2, 159.3, 157.2, 153.7, 143.2, 136.3, 134.8, 133.7, 132.9, 131.3, 130.5, 130.3, 130.0, 129.8, 128.2, 127.7, 124.0, 122.3, 121.4, 113.0, 110.1, 61.8, 51.5, 35.8. IR (KBr): 1705 (C=O), 1506, 1227, 1129 cm^{-1}. MS (70 eV) m/z (%): 532 (M^+, 18), 499 (16), 397 (100), 328 (16), 255 (23), 205 (17), 145 (80), 130 (20), 102 (29). Anal. Calcd for $C_{28}H_{21}ClN_2O_5S$ (533.0): C, 63.10; H, 3.97; N, 5.26. Found: C, 63.01; H, 4.10; N, 5.11.

Bioassays of Fungicidal Activity

The fungicidal activities against six kinds of fungi, *Fusarium oxysporium*, *Rhizoctonia solani*, *Botrytis cinereapers*, *Gibberella zeae*, *Dothiorella gregaria*, *Bipolaris mayclis*, and *Colletotrichum gossypii*, were tested according to the reported method.[21] (See the Supplemental Materials.)

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