Synthesis and Fungicidal Activity of 5-Aryl-1-(aryloxyacetyl)-3-(*tert*-butyl or phenyl)-4-(1*H*-1,2,4-triazol-1-yl)-4,5-dihydropyrazole

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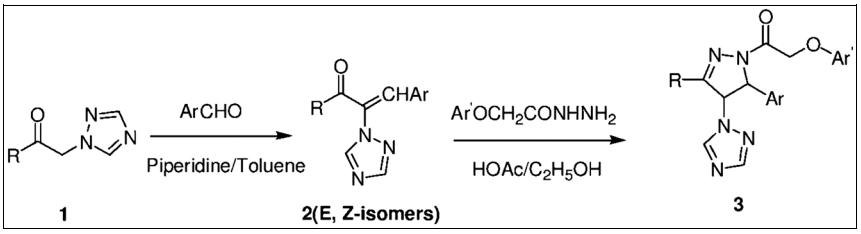

A series of novel 5-aryl-1-(aryloxyacetyl)-3-(*tert*-butyl or phenyl)-4-(1*H*-1,2,4-triazol-1-yl)-4,5-dihydropyrazole **3a**–**3n** were synthesized by the annulation of 2-aryloxyacetohydrazides with 3-aryl-1-*t*-butyl (or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-ones (**2**) in the presence of a catalytic amount of acetic acid. Compounds **2** were obtained by the Knoevenagel reactions of 1-*t*-butyl (or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone (**1**) with aromatic aldehydes in the presence of piperidine. Their structures were confirmed by IR, ^{1}H-NMR, ESI-MS, and elemental analyses. The preliminary bioassay indicated that some compounds displayed moderate to excellent fungicidal activity. For example, compounds **3l**, **3m**, and **3n** possessed 100% inhibition against *Cercospora arachidicola* Hori at the concentration of 50 mg/L.

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INTRODUCTION

Many arylpyrazole and pyrazoline derivatives were widely used as agrochemicals such as fungicides, herbicides and insecticides in plant protection or in pharmaceuticals [1–7]. Recently, the triazole fungicides, as an important class of agrochemicals, have played a major role in crop protection [8–10]. The introduction of these sterol biosynthesis inhibitors represented a significant progress in the chemical control of fungal diseases. More than 30 triazole fungicides such as Uniconazole, Diniconazole and Paclobutrazol, have been commercialized. To find novel triazole fungicides with high activity and low toxicity, we designed and synthesized a series of novel target compounds **3** via the annulation of 2-aryloxyacetohydrazides with 3-aryl-1-*t*-butyl (or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-ones, in which the triazole ring was linking with a pyrazoline ring in the same molecular skeleton. Herein, we would like to report the synthesis and fungicidal activities of the title compounds **3** in this article (Scheme 1).

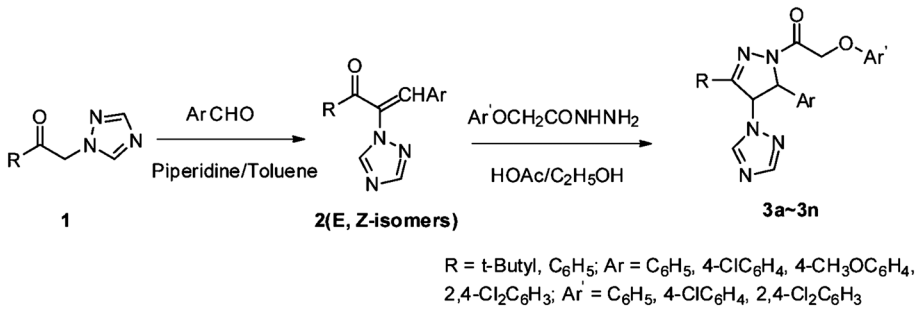
RESULTS AND DISCUSSION

1-(*t*-Butyl or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone (**1**) reacted with aromatic aldehydes in the presence of piperidine to obtain 3-aryl-1-*t*-butyl(or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-ones (**2**) as Z- and E-isomer mixtures. Treatment of **2** with 2-aryloxyacetohydrazides in the presence of a catalytic amount of glacial acetic acid in ethanol medium at room temperature afforded 5-aryl-1-(aryloxyacetyl)-3-(*tert*-butyl or phenyl)-4-(1*H*-1,2,4-triazol-1-yl)-4,5-dihydropyrazole **3** in moderate to excellent yields.

Their structures were deduced from their spectral data (IR, ^{1}H-NMR, and ESI-MS) and elemental analyses, which were listed in the experimental part. In the ^{1}H-NMR spectra of **3**, the *t*-butyl protons displayed as a singlet with chemical shift δ between 0.79 and 1.21; the methylene protons showed as a singlet, sometimes as AB system with chemical shifts δ 4.4, the two methine protons of pyrazoline ring exhibited as two doublets with coupling constants of about 9.0 Hz in δ 4.8 and 5.7, respectively; whereas the 1,2,4-triazole protons showed two singlets with chemical shifts δ 8.0 and 8.6, respectively. IR spectra of compounds **3** showed normal stretching absorption bands, indicating the existence Ar-H (~2960 cm^{-1}), C═O (~1690 cm^{-1}), C═N (~1640 cm^{-1}), C—O—C (~1050 cm^{-1}). The ESI mass spectra of compounds **3** revealed the existence of the molecular ion peaks and strong M+K-1 or M+Na-1 peaks, which were in good accordance with the given structures of products.

Fungicidal activity. The preliminary fungicidal activity of the target compounds **3** was evaluated by the classic plate method at the concentration of 50 mg/L, which was described in the experimental part. The five fungi used, *Fusarium oxysporium, Physalospora piricola* Nose, *Alternaria solani, Cercospora arachidicola* Hori, and *Gibberella sanbinetti*, belong to the group of field fungi

Scheme 1. Synthetic route to compounds **3a–3n**.



and were isolated from corresponding crops. The activities data were also listed in Table 1. The preliminary bioassay (*in vitro*) indicated that some of the title compounds **3** exhibited moderate to good inhibitory activities against the above five fungi. For example, compounds **3i, 3l**, and **3n** possessed 81.8%, 81.8%, and 95.5% inhibition against *Fusarium oxysporium*, respectively, and compound **3n** exhibited 89.3% inhibition against *Physalospora piricola* Nose. Moreover, compounds **3l**, **3m**, and **3n** possessed 100% inhibition against *Cercospora arachidicola* Hori as well as the control drug-difenoconazole did at the concentration of 50 mg/L. However, most of compounds **3** exhibited weaker fungicidal activities against the tested fungi than the control drug—difenoconazole did. As for the preliminary structure-activity relationships, first, the compounds whose R is *tert*-butyl showed better activities than those whose R is phenyl did. Secondly, when Ar and Ar′ are both 2,4-dichlorophenyl, the compound showed the best activities against those fungi. Further exploring of structure-activity relationships needs more experimental results to support. Further biological activity (*in vivo*) investigations are on the way.

In conclusion, a series of novel 5-aryl-1-(aryloxyacetyl)-3-(*tert*-butyl or phenyl)-4-(1*H*-1,2,4-triazol-1-yl)-4,5-dihydropyrazole **3a**–**3n** were synthesized by the annulation of 2-aryloxyacetohydrazides with 3-aryl-1-*t*-butyl (or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-ones (**2**) in the presence of a catalytic amount of acetic acid. The preliminary bioassay indicated that some of the title compounds exhibited good fungicidal activities against five fungi used, and the compounds **3l**, **3m**, and **3n** possessed 100% inhibition against *Cercospora arachidicola* Hori at the concentration of 50 mg/L.

EXPERIMENTAL

Melting points were determined with a WRS-1B digital melting point apparatus and are uncorrected. ^{1}H-NMR spectra was recorded with a Varian Mercury PLUS 600 (600 MHz) spectrometer with TMS as the internal reference and $CDCl_3$ as the solvent, while mass spectra were obtained with an Applied Biosystems API 2000 LC/MS/MS (ESI-MS) spectrometer. IR spectra were measured by a Nicolet NEXUS470 spectrometer. Elemental analyses were performed with an Elementar Vario ELIII CHNSO elemental analyzer. 3-Aryl-1-*t*-butyl (or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-one (**2**) were prepared by the Knoevenagel reactions of 1-*tert*-butyl

Table 1

Fungicidal activity of compounds 3a–3n (*in vitro*, 50 mg/L, relative inhibitory rate %).

Compd.	*Fusarium oxysporium*	*Physalospora piricola* Nose	*Alternaria solani*	*Cercospora arachidicola* Hori	*Gibberella sanbinetti*
3a	31.8	25.0	25.0	38.5	41.4
3b	22.7	17.9	14.3	15.4	27.6
3c	18.2	0	21.4	23.1	15.5
3d	45.5	39.3	46.4	69.2	51.7
3e	22.7	39.3	25.0	53.8	39.7
3f	27.3	7.1	21.4	30.8	20.7
3g	63.6	25.0	21.4	46.2	32.8
3h	77.3	7.1	10.7	76.9	32.8
3i	81.8	0.0	7.1	61.5	15.5
3j	27.3	50.0	46.4	61.5	51.7
3k	0.0	17.9	14.3	46.2	24.1
3l	81.8	78.6	71.4	100	87.9
3m	77.3	78.6	67.9	100	87.9
3n	95.5	89.3	67.9	100	86.2
Difenoconazole	100	100	100	100	98.3

(or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)-ethanone (**1**) with aromatic aldehydes in the presence of piperidine according to the literature procedure [11]. 2-Aryloxyacetohydrazides were synthesized using the reported method [12]. All of the solvents and materials were reagent grade and purified as required.

General procedure for the synthesis of 5-aryl-1-(aryloxyacetyl)-3-(*tert*-butyl or phenyl)-4-(1H-1,2,4-triazol-1-yl)-4,5-dihydropyrazole 3. 3-aryl-1-*t*-butyl (or phenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-one **2** (2.0 mmol), 2-aryloxyacetohydrazides (2.4 mmol), anhydrous ethanol (20 mL) and several drops of glacial acetic acid were added to a 50 mL three-necked flask, the mixture was stirred at room temperature for 6–10 h till the reaction was completed (monitored by TLC). The solid was filtered and recrystallized by anhydrous ethanol to give the target compounds **3a–3n** in 56–87% yields.

3a (R = *t*-butyl, Ar = 2,4-$Cl_2C_6H_3$, Ar′ = C_6H_5): white crystals, yield: 56%, m.p. 141.2–141.5°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 1.21 (s, 9H, $3CH_3$), 4.47 (s, 2H, CH_2), 5.23 (d, *J* = 9.0 Hz, 1H, CH), 5.96 (d, *J* = 9.0 Hz, 1H, CH), 6.82 (d, *J* = 7.8 Hz, 2H, ArH), 7.02–7.30 (m, 5H, ArH), 7.79(s, 1H, triazole-H), 7.84 (s, 1H, Ar—H), 8.05 (s, 1H, triazole-H); IR (KBr) υ: 3071, 2971 (ArH), 1715 (C═O), 1652 (C═N), 1592, 1495, 1477 (Ar), 1218, 1061(C—O—C) cm^{-1}; ESI-MS *m/z* (%): 512 (M+K+2, 100), 510 (M+K, 85), 494 (M+Na, 16), 472 (M^++1, 8), 347 (26). Anal. calcd for $C_{23}H_{23}Cl_2N_5O_2$: C 58.48, H 4.91, N 14.83; found C 58.30, H 4.84, N 14.97.

3b (R = *t*-butyl, Ar = 2,4-$Cl_2C_6H_3$, Ar′ = 4-ClC_6H_4): white solid, yield: 80%, m.p. 144.6–146.4°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 1.13 (s, 9H, $3CH_3$), 4.44 (s, 2H, CH_2), 5.19 (d, *J* = 8.4 Hz, 1H, CH), 5.93 (d, *J* = 9.0 Hz, 1H, CH), 6.75 (d, *J* = 8.4 Hz, 2H, ArH), 7.09–7.30 (m, 4H, ArH), 7.76 (s, 1H, triazole-H), 7.82 (s, 1H, Ar—H), 8.09 (s, 1H, triazole-H); IR (KBr) υ: 3123, 2972 (ArH), 1716 (C═O), 1643 (C═N), 1508, 1491, 1368 (Ar), 1276, 1220, 1057(C—O—C) cm^{-1}; ESI-MS *m/z* (%): 547.6 (M+K+2, 100), 546 (M+K, 89), 507 (M^++2, 8), 505 (5). Anal. calcd for $C_{23}H_{22}Cl_3N_5O_2$: C 54.51, H 4.38, N 13.82; found C 54.73, H 4.24, N 13.67.

3c (R = *t*-butyl, Ar = 2,4-$Cl_2C_6H_3$, Ar′ = 2,4-$Cl_2C_6H_3$): white crystals, yield: 72%, m.p. 156.1–156.5°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 1.15 (s, 9H, $3CH_3$), 4.50 (s, 2H, CH_2), 5.26 (d, *J* = 9.0 Hz, 1H, CH), 5.94 (d, *J* = 9.0 Hz, 1H, CH), 6.71 (d, *J* = 8.4 Hz, 1H, ArH), 7.17 (d, *J* = 8.4 Hz, 2H, ArH), 7.29 (d, *J* = 8.4 Hz, 1H, ArH), 7.38 (s, 1H, ArH), 7.80 (s, 1H, triazole-H), 7.94 (s, 1H, ArH), 8.05 (s, 1H, triazole-H); IR (KBr) υ: 3126, 2974 (ArH), 1718 (C═O), 1636 (C═N), 1588, 1476, 1363 (Ar), 1236, 1071(C—O—C) cm^{-1}; ESI-MS *m/z* (%): 582 (M+K+2, 86), 580 (M+K, 100), 543 (M^++2, 4), 541 (3). Anal. calcd for $C_{23}H_{21}Cl_4N_5O_2$: C 51.04, H 3.91, N 12.94; found C 51.23, H 4.07, N 12.70.

3d (R = *t*-butyl, Ar = 4-ClC_6H_4, Ar′ = C_6H_5): white solid, yield: 78%, m.p. 130.0–131.8°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.84 (s, 9H, $3CH_3$), 4.40 (s, 2H, CH_2), 4.87 (d, *J* = 9.0 Hz, 1H, CH), 5.69 (d, *J* = 8.4 Hz, 1H, CH), 6.76 (d, *J* = 6.6 Hz, 2H, ArH), 7.00 (t, *J* = 7.2 Hz, 1H, ArH), 7.28–7.41 (m, 6H, ArH), 7.98 (s, 1H, triazole-H), 8.60 (s, 1H, triazole-H); IR (KBr) υ: 3124, 2972 (ArH), 1715 (C═O), 1639 (C═N), 1586, 1477, 1365 (Ar), 1233, 1067 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 478 (M+K+1, 89), 437 (M^+, 5), 311 (100), 190 (45). Anal. calcd for $C_{23}H_{24}ClN_5O_2$: C 63.08, H 5.52, N 15.99; found C 62.95, H 5.37, N 15.72.

3e (R = *t*-butyl, Ar = 4-ClC_6H_4, Ar′ = 4-ClC_6H_4): white crystals, yield: 65%, m.p. 168.1–169.2°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.83 (s, 9H, $3CH_3$), 4.36 (s, 2H, CH_2), 4.82 (d, *J* = 9.0 Hz, 1H, CH), 5.68 (d, *J* = 9.0 Hz, 1H, CH), 6.68 (d, *J* = 9.0 Hz, 2H, ArH), 7.20 (d, *J* = 9.0 Hz, 2H, ArH), 7.25 (d, *J* = 9.0 Hz, 2H, ArH), 7.30 (d, *J* = 8.4 Hz, 2H, ArH), 7.96 (s, 1H, triazole-H), 8.55 (s, 1H, triazole-H); IR (KBr) υ: 3115, 2973 (ArH), 1700 (C═O), 1659 (C═N), 1580, 1492, 1368 (Ar), 1273, 1224, 1093 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 514 (M+K+4, 35), 512 (M+K+2, 100), 510 (M +K, 40). Anal. calcd for $C_{23}H_{23}Cl_2N_5O_2$: C 58.48, H 4.91, N 14.83; found C 58.40, H 5.06, N 14.98.

3f (R = *t*-butyl, Ar = 4-ClC_6H_4, Ar′ = 2,4-$Cl_2C_6H_3$): white crystals, yield: 87%, m.p. 155.5–157.2°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.83 (s, 9H, $3CH_3$), 4.40 (AB, *J* = 14.4 Hz, 2H, CH_2), 4.87 (d, *J* = 9.6 Hz, 1H, CH), 5.69 (d, *J* = 9.0 Hz, 1H, CH), 6.68 (d, *J* = 8.4 Hz, 1H, ArH), 7.14 (d, *J* = 8.4 Hz, 1H, ArH), 7.15 (d, *J* = 8.4 Hz, 2H, ArH), 7.32 (d, *J* = 8.4 Hz, 2H, ArH), 7.61 (s, 1H, ArH), 7.96 (s, 1H, triazole-H), 8.51 (s, 1H, triazole-H); IR (KBr) υ: 3128, 2974 (ArH), 1712 (C═O), 1656 (C═N), 1579, 1477, 1321 (Ar), 1232, 1071 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 548 (M+K+4), 546 (M+K, 100), 381 (25), 379 (17). Anal. calcd for $C_{23}H_{22}Cl_3N_5O_2$: C 54.51, H 4.38, N 13.82; found C 54.71, H 4.44, N 13.69.

3g (R = *t*-butyl, Ar = C_6H_5, Ar′ = C_6H_5): white solid, yield: 75%, m.p. 129.3–131.8°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.79 (s, 9H, $3CH_3$), 4.38 (s, 2H, CH_2), 4.86 (d, *J* = 8.4 Hz, 1H, CH), 5.73 (d, *J* = 9.0 Hz, 1H, CH), 6.75 (d, *J* = 8.4 Hz, 2H, ArH), 6.99 (t, *J* = 8.4 Hz, 1H, ArH), 7.24–7.42 (m, 7H, ArH), 7.96 (s, 1H, triazole-H), 8.56 (s, 1H, triazole-H); IR (KBr) υ: 3113, 2971 (ArH), 1705 (C═O), 1655 (C═N), 1582, 1496, 1364 (Ar), 1270, 1226, 1084 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 444 (M+K+2, 35), 442 (M+K, 36), 277 (86). Anal. calcd for $C_{23}H_{25}N_5O_2$: C 68.47, H 6.25, N 17.36; found C 68.61, H 6.18, N 17.50.

3h (R = *t*-butyl, Ar = C_6H_5, Ar′ = 4-ClC_6H_4): white solid, yield: 74%, m.p. 140.1–141.8°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.80 (s, 9H, $3CH_3$), 4.36 (s, 2H, CH_2), 4.84 (d, *J* = 8.4 Hz, 1H, CH), 5.73 (d, *J* = 9.0 Hz, 1H, CH), 6.68 (d, *J* = 8.4 Hz, 2H, ArH), 7.19 (d, *J* = 8.4 Hz, 2H, ArH), 7.31–7.36 (m, 5H, ArH), 7.96 (s, 1H, triazole-H), 8.62 (s, 1H, triazole-H); IR (KBr) υ: 3115, 2977 (ArH), 1699 (C═O), 1655 (C═N), 1582, 1491, 1329 (Ar), 1276, 1221, 1059 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 479 (88), 477 (M+K+1, 100), 311 (97). Anal. calcd for $C_{23}H_{24}ClN_5O_2$: C 63.08, H 5.52, N 15.99; found C 63.24, H 5.77, N 16.13.

3i (R = *t*-butyl, Ar = C_6H_5, Ar′ = 2,4-$Cl_2C_6H_3$): white solid, yield: 67%, m.p. 154.2–155.8°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.79 (s, 9H, $3CH_3$), 4.40 (AB, *J* = 15.0 Hz, 2H, CH_2), 4.88 (d, *J* = 9.6 Hz, 1H, CH), 5.74 (d, *J* = 9.6 Hz, 1H, CH), 6.66 (d, *J* = 9.0 Hz, 1H, ArH), 7.12 (d, *J* = 9.0 Hz, 1H, ArH), 7.28–7.33 (m, 5H, ArH), 7.64 (s, 1H, ArH), 7.96 (s, 1H, triazole-H), 8.58 (s, 1H, triazole-H); IR (KBr) υ: 3134, 2972 (ArH), 1720 (C═O), 1652 (C═N), 1531, 1500, 1473, 1348 (Ar), 1292, 1230, 1074 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 512 (M+K+2, 100), 510 (M+K, 26). Anal. calcd for $C_{23}H_{23}Cl_2N_5O_2$: C 58.48, H 4.91, N 14.83; found C 58.31, H 4.75, N 14.62.

3j (R = *t*-butyl, Ar = 4-$CH_3OC_6H_4$, Ar′ = 4-ClC_6H_4): white solid, yield: 75%, m.p. 115.8–116.9°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.80 (s, 9H, $3CH_3$), 3.73 (s, 3H, CH_3O), 4.55 (s, 2H, CH_2), 4.79 (d, *J* = 9.6 Hz, 1H, CH), 5.69 (d, *J* = 9.0 Hz, 1H, CH), 6.68 (d, *J* = 9.0 Hz, 2H, ArH), 6.84 (d, *J* = 9.0 Hz, 2H, ArH), 7.19–7.23 (m, 4H, ArH), 7.95 (s, 1H, triazole-H), 8.55 (s, 1H, triazole-H); IR (KBr) υ: 3120, 2967 (ArH), 1717 (C═O), 1681 (C═N), 1631, 1513, 1490 (Ar), 1250, 1218, 1061 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 507.6 (M+K+1, 100), 507 (M+K, 87), 340.6 (52). Anal. calcd for $C_{24}H_{26}ClN_5O_3$: C 61.60, H 5.60, N 14.97; found C 61.73, H 5.66, N 14.82.

3k (R = *t*-butyl, Ar = 4-$CH_3OC_6H_4$, Ar′ = 2,4-$Cl_2C_6H_3$): white solid, yield: 84%, m.p. 149.5–151.5°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.81 (s, 9H, $3CH_3$), 3.80 (s, 3H, CH_3O), 4.40 (AB, *J* = 15.0 Hz, 2H, CH_2), 4.83 (d, *J* = 9.6 Hz, 1H, CH), 5.71 (d, *J* = 9.0 Hz, 1H, CH), 6.66 (d, *J* = 9.0 Hz, 1H, ArH), 6.85 (d, *J* = 9.0 Hz, 2H, ArH), 7.14 (d, *J* = 8.4 Hz, 1H, ArH), 7.24 (d, *J* = 8.4 Hz, 2H, ArH), 7.31 (s, 1H, ArH), 7.96 (s, 1H, triazole-H), 8.53 (s, 1H, triazole-H); IR (KBr) υ: 3076, 2969 (ArH), 1720 (C═O), 1662 (C═N), 1515, 1476, 1392 (Ar), 1249, 1232, 1076 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 542 (M+K+2, 100), 541 (M+K+1, 67), 520 (45), 508 (21), 353 (35). Anal. calcd for $C_{24}H_{25}Cl_2N_5O_3$: C 57.38, H 5.02, N 13.94; found C 57.20, H 4.93, N 14.07.

3l (R = C_6H_5, Ar = 2,4-$Cl_2C_6H_3$, Ar′ = C_6H_5): white solid, yield: 68%, m.p. 121.9–123.4°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 4.25 (AB, *J* = 15.0 Hz, 2H, CH_2), 5.21 (d, *J* = 6.6 Hz, 1H, CH), 5.45 (d, *J* = 6.0 Hz, 1H, CH), 6.79–7.04 (m, 5H, ArH), 7.27–7.73 (m, 7H, ArH), 7.79 (s, 1H, triazole-H), 8.03(s, 1H, ArH), 8.81 (s, 1H, triazole-H); IR (KBr) υ: 3061, 2959 (ArH), 1694 (C═O), 1598 (C═N), 1494, 1448, 1332 (Ar), 1251, 1140, 1057 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 530 (M+K, 100), 510 (63), 377 (75). Anal. calcd for $C_{25}H_{19}Cl_2N_5O_2$: C 60.99, H 3.89, N 14.22; found C 60.84, H 4.05, N 14.13.

3m (R = C_6H_5, Ar = 2,4-$Cl_2C_6H_3$, Ar′ = 4-ClC_6H_4): white crystals, yield: 66%, m.p. 118.6–120.5°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 4.24 (AB, *J* = 15.6 Hz, 2H, CH_2), 5.43 (d, *J* = 6.6 Hz, 1H, CH), 6.42 (d, *J* = 6.6 Hz, 1H, CH), 6.71 (d, *J* = 8.4 Hz, 2H, ArH), 6.81 (d, *J* = 9.0 Hz, 1H, ArH), 7.02 (d, *J* = 9.0 Hz, 1H, ArH), 7.22–7.63 (m, 5H, ArH), 7.70 (s, 1H, ArH), 7.80 (s, 1H, triazole-H), 8.03 (d, *J* = 8.4 Hz, 2H, ArH), 8.83 (s, 1H, triazole-H); IR (KBr) υ: 3068, 2963 (ArH), 1696 (C═O), 1564 (C═N), 1495, 1442, 1336 (Ar), 1250, 1144, 1052 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 566 (M+K+2, 52), 549 (M+Na+1, 100), 528 (82). Anal. calcd for $C_{25}H_{18}Cl_3N_5O_2$: C 57.00, H 3.44, N 13.29; found C 57.17, H 3.56, N 13.48.

3n (R = C_6H_5, Ar = 2,4-$Cl_2C_6H_3$, Ar′ = 2,4-$Cl_2C_6H_3$): white solid, yield: 58%, m.p. 130.1–132.1°C; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 4.34 (AB, *J* = 15.0 Hz, 2H, CH_2), 5.42 (d, *J* = 6.0 Hz, 1H, CH), 6.41 (d, *J* = 6.6 Hz, 1H, CH), 6.65 (d, *J* = 9.0 Hz, 1H, ArH), 6.86 (d, *J* = 8.4 Hz, 1H, ArH), 7.04 (d, *J* = 9.0 Hz, 1H, ArH), 7.16 (d, *J* = 8.4 Hz, 1H, ArH), 7.35 (s, 1H, ArH), 7.39 (s, 1H, ArH), 7.45–7.65 (m, 3H, ArH), 7.79 (s, 1H, triazole-H), 7.84 (d, *J* = 7.2 Hz, 1H, ArH), 8.03 (d, *J* = 7.2 Hz, 1H, ArH), 8.73 (s, 1H, triazole-H); IR (KBr) υ: 3060, 2959 (ArH), 1693 (C═O), 1589 (C═N), 1479, 1439, 1386 (Ar), 1264, 1139, 1068 (C—O—C) cm^{-1}; ESI-MS *m/z* (%): 601 (M+K+2, 64), 599.6 (M+K+1, 100), 578 (48), 377 (65). Anal. calcd for $C_{25}H_{17}Cl_4N_5O_2$: C 53.50, H 3.05, N 12.48; found C 53.31, H 3.08, N 12.65.

Fungicidal activity testing. The fungicidal activity measurement method was adopted from the one described by Molina Torres [13]. The synthesized target compounds were dissolved in 0.5–1.0 mL of DMF to the concentration of 500 mg/L. The solutions (1 mL) were mixed rapidly with thawed potato glucose agar culture medium (9 mL) under 50°C. The mixtures were poured into Petri dishes. After the dished were cooled, the solidified plates were incubated with 4 mm mycelium disk, inverted, and incubated at 28°C for 48 h. Distilled water was used as the blank control and the commercially available fungicide difenoconazole as the control drug. Three replicates of each test were carried out. The mycelial elongation radius (mm) of fungi settlements was measured after 48 h of culture. The growth inhibitory rates were calculated with the following equation: $I = [(C\text{-}T)/C] \times 100\%$. Here, *I* is the growth inhibitory rate (%), *T* is the treatment group fungi settlement radius (mm) and *C* is the radius of the blank control. The results are listed in Table 1.

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