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Research Article

Synthesis and Biological Activities of Some Novel (*E*)-Alpha-(methoxyimino)benzeneacetate Derivatives with Modified 1,2,4-Triazole Moiety

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To find new strobilurin analogues with high activity against resistant pathogens, a series of (*E*)-α-(methoxyimino)benzeneacetate derivatives containing 1,2,4-triazole Schiff base side chain were designed and synthesized. Their structures were confirmed by IR, ^{1}H NMR, and ^{13}C NMR, ESI-HRMS, or elemental analyses. Bioassays indicated that most of the target compounds showed moderate to good fungicidal activities against *Rhizoctonia solani*, *Botrytis cinerea Pers.*, *Fusarium graminearum*, *Cotton rhizoctoniosis*, and *Blumeria graminis*. For example, compounds **6g** and **6j** exhibited promising antifungal activity against *Rhizoctonia solani*, *Botrytis cinerea Pers.,* and *Fusarium graminearum*. Compounds **6c**, **6l**, and **6m** had higher fungicidal activities against *Blumeria graminis* at the concentration of 50 μg/mL; inhibitory rate is 91.41%, 92.13%, and 91.77%, respectively.

1. Introduction

The strobilurins, derived from fermentations of *Strobilurus tenacellus* by Anke and coworkers in 1977, are one of the most important classes of agricultural fungicides [1]. Their primary mechanism of action is the inhibition of mitochondrial respiration by blocking electron transfer at the ubiquinol oxidation center (Q_o site) of the cytochrome bc_1 complex (complex III) [2].

Strobilurin derivatives have attracted significant attention of the agricultural chemists owing to their outstanding characteristics and unique mode of action, broader antifungal spectrum, long-lasting effects, high antifungal activity, and low toxicity toward mammalian cells [3–6]. The strobilurins were first commercialized in 1996 with the launch of azoxystrobin and kresoxim-methyl (Figure 1) [7]. Till date, over ten strobilurin derivatives are commercially available [8–10]. However, following the use of strobilurin fungicides in a short period of field applications, significant increase in resistance to fungicide has been observed [11].

Recently, significant research efforts focusing on structural modification of strobilurins have been devoted to overcoming the above-mentioned problem. Moreover, according to the literature, the methoxyiminoacetate is an effective pharmacophore which is indispensable for antifungal activity of strobilurin fungicides. The aromatic bridge helps to stabilize the molecule and the molecule also exhibits photo stability. Therefore, numerous studies have reported that modification of the side chain is the most effective method to obtain novel strobilurin derivatives with higher biological activities [6, 12–14].

In general, 1,2,4-triazole and similar Schiff bases exhibit diverse biological activities, such as pesticides, fungicides, herbicidal, anticancer, anti-inflammatory, antiviral, and antimicrobial properties [15–22]. So far, over twenty triazole fungicides have been commercialized, like triadimefon and triadimenol (Figure 1). Therefore, based on the active substructure combination and bioisosteric replacement, the intermediate derivatization method was employed to synthesize a series of novel strobilurin derivatives containing 1,2,4-triazole

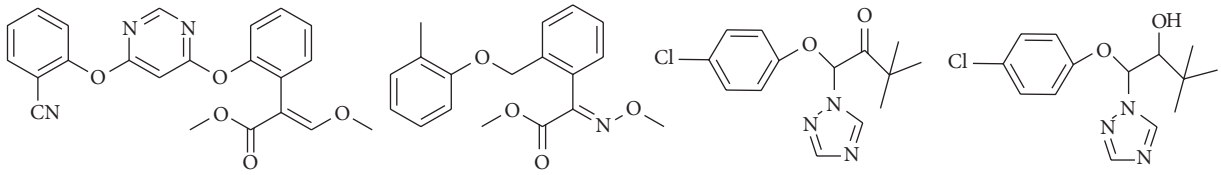


Figure 1: Structures of azoxystrobin, kresoxim-methyl, triadimefon, and triadimenol.

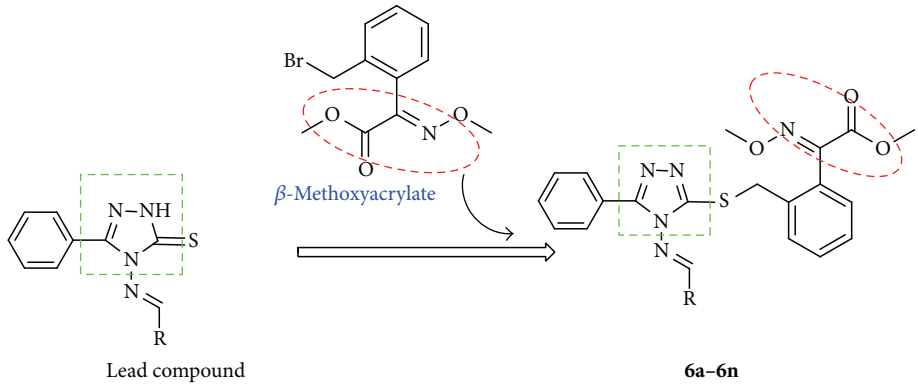


Figure 2: Design strategy of the title compounds.

moieties. Moreover, strobilurin pharmacophores were designed and synthesized with the objective of obtaining more active candidates against resistant fungal strains (Figure 2). The results of bioassays revealed that most of the (*E*)-*α*-(methoxyimino)benzeneacetate derivatives exhibited potential antifungal activities against *Rhizoctonia solani*, *Botrytis cinerea Pers.*, *Fusarium graminearum*, *Cotton rhizoctoniosis*, and *Blumeria graminis*.

2. Experimental

2.1. General Information. All melting points were determined on an XT-4A apparatus and are uncorrected. The IR spectra (KBr disks) were taken on a Bruker Equinox 55 spectrophotometer. The ^{1}H NMR spectra were measured on a Bruker Advance 600 spectrometer for DMSO-*d6* solutions using TMS as internal standard. Elemental analyses were determined on a Flash-1112 series elemental analyzer. All the reagents used were AR grade. Molecular weights of monomers were determined by high resolution mass spectroscopy (ESI-HRMS, Bruker daltonics apexultra 7.0 tesla Fourier transform ion cyclotron resonance mass spectrometer). The completion of reactions was monitored by TLC.

*2.2. General Procedure for the Synthesis of Benzohydrazide (**2**) [23].* A mixture of ethyl benzoate **1** (0.1 mol) and hydrazine hydrate (0.1 mol) in ethanol (30 mL) was stirred vigorously for 6 h at room temperature. The mixture was filtered, and the solid was washed with cold water, dried, and recrystallized from ethanol to give intermediate **2**, white crystal, yield: 90.6%, m.p.: 112–114°C.

*2.3. General Method for the Synthesis of Potassium Dithiocarbazinate (**3**) [24].* Potassium hydroxide (0.15 mol) was dissolved in absolute ethanol (100 mL) followed by the addition of benzohydrazide **2** (0.1 mol). The resulting solution was cooled in ice. Subsequently, carbon disulfide (0.15 mol) was added dropwise, and the reaction mixture was stirred for 15 h at room temperature. The precipitated potassium dithiocarbazinate was collected by filtration. The precipitate was further washed with anhydrous ether (100 mL), dried, and used directly without purification for the subsequent reaction.

*2.4. Synthesis of 4-Amino-3-phenyl-5-thiol-1,2,4-triazole (**4**) [25].* Potassium dithiocarbazinate **3** (0.5 mol) was added to hydrazine hydrate (0.15 mmol) and refluxed for 6 h with occasional shaking. The color of the reaction mixture changed to green with the evolution of hydrogen sulfide gas (lead acetate paper test and odor). The reaction mixture was cooled to room temperature and diluted with water. On acidification with concentrated hydrochloric acid, the corresponding triazole was precipitated. It was filtered, washed thoroughly with cold water, and recrystallized from ethanol to give 4-amino-3-phenyl-5-thiol-1,2,4-triazole **4**. White crystal, yield: 63.1%, m.p.: 201-202°C; IR (KBr, cm^{-1}): 3412, 3070, 2667, 1640. ^{1}H NMR (600 MHz, DMSO-*d6*) δ: 13.90 (s, 1H, triazole–NH), 7.52–8.01 (m, 5H, Ar-H), 5.81 (s, 2H, NH_2).

*2.5. General Method for the Preparation of (E)-3-Thiol-4-arylideneamino-5-phenyl-4H-1,2,4-triazole (**5a–5n**).* Appropriate benzaldehyde (10 mmol) and 2 to 3 drops of glacial acetic acid were added to a solution of compound **4** (10 mmol)

dissolved in absolute alcohol (30 mL). The mixture was refluxed for 4 h with stirring. The solid that was obtained on cooling was filtered, washed with cold water, dried, and recrystallized from alcohol to give a series of Schiff bases **5a**–**5n**.

*(E)-3-Thiol-4-benzylideneamino-5-phenyl-4H-1,2,4-triazole (**5a**)*. White powder, yield: 70.0%, m.p.: 180-181°C. IR (KBr, cm^{-1}): 3102, 2974, 1610, 1554, 1530, 1482, 1269. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.43–7.71 (m, 6H, Ar-H), 7.90 (d, J = 7.8 Hz, 4H, Ar-H), 9.71 (s, 1H, CH=N), 14.25 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 127.71, 128.22, 128.26, 128.33, 128.44, 129.47, 130.85, 134.39, 144.82, 154.73, 165.12. Anal. calcd for $C_{15}H_{12}N_4S$: C, 64.26; H, 4.31; N, 19.98; found: C, 64.31; H, 4.29; N, 19.93.

*(E)-3-Thiol-4-(4-methylbenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5b**)*. Red solid, yield: 62.5%, m.p.: 239-240°C. IR (KBr, cm^{-1}): 3110, 2979, 1618, 1516, 1512, 1484, and 1271. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 2.41 (s, 3H, CH_3), 7.46–7.58 (m, 3H, Ar-H), 7.66 (t, J = 13.6 Hz, 2H, Ar-H), 7.86 (dd, J = 13.2, 11.7 Hz, 2H, Ar-H), 7.92 (d, J = 8.4 Hz, 2H, Ar-H), 9.62 (s, 1H, CH=N), 14.21 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 21.16, 128.03, 128.22, 128.25, 128.42, 128.61, 130.82, 131.71, 137.95, 144.87, 154.73, 165.12. Anal. calcd for $C_{16}H_{14}N_4S$: C, 65.28; H, 4.79; N, 19.03; found: C, 65.33; H, 4.77; N, 18.99.

*(E)-3-Thiol-4-(4-dimethylaminobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5c**)*. White solid, yield: 75.1%, m.p.: 233-234°C. IR (KBr, cm^{-1}): 3113, 2978, 1613 1552 1531, 1482, 1275. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.34 (s, 6H, N-$(CH_3)_2$), 7.09 (t, J = 7.3 Hz, 1H, Ar-H), 7.22 (d, J = 8.4 Hz, 1H, Ar-H), 7.44–7.70 (m, 4H, Ar-H), 7.90–7.92 (m, 3H, Ar-H), 9.50 (s, 1H, CH=N), 14.28 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 41.92, 111.93, 120.04, 128.22, 128.24, 128.27, 128.42, 130.84, 144.84, 153.11, 154.72, 165.11. Anal. calcd for $C_{17}H_{17}N_5S$: C, 63.13; H, 5.30; N, 21.65; found: C,63.20; H, 5.26; N, 21.59.

*(E)-3-Thiol-4-(2-hydroxylbenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5d**)*. White needle crystal, yield: 78.4%, m.p.: 195-196°C. IR (KBr, cm^{-1}): 3122, 3102, 2977, 1620, 1550, 1531, 1486, 1269. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 6.82–7.10 (m, 2H, Ar-H), 7.45 (t, J = 7.7 Hz, 1H, Ar-H), 7.54–7.56 (m, 3H, Ar-H), 7.73–7.93 (m, 3H, Ar-H), 9.65 (s, 1H, CH=N), 10.47 (s, 1H, Ar-OH), 14.21 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 116.25, 119.62, 121.01, 128.24, 128.24, 128.46, 129.65, 130.86, 131.03, 144.85, 146.81, 159.93, 165.12. Anal. calcd for $C_{15}H_{12}N_4OS$: C, 60.79; H, 4.08; N, 18.91; found: C, 60.73; H, 4.10; N, 18.94.

*(E)-3-Thiol-4-(3-hydroxylbenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5e**)*. White needle crystal, yield: 65.8%, m.p.: 205-206°C. IR (KBr, cm^{-1}): 3120, 3100, 2987, 1622, 1549, 1536, 1487, 1278. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.02–7.20 (m, 2H, Ar-H), 7.49 (t, J = 7.6 Hz, 1H, Ar-H), 7.52–7.61 (m, 4H, Ar-H), 7.76–7.98 (m, 2H, Ar-H), 9.65 (s, 1H, CH=N), 10.42 (s, 1H, Ar-OH), 14.22 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 115.09, 117.22, 120.90, 128.21, 128.24, 128.42, 130.41, 130.87, 136.96, 144.85, 155.92, 157.36, 165.12. Anal. calcd for $C_{15}H_{12}N_4OS$: C, 60.79; H, 4.08; N, 18.91; found: C, 60.71; H, 4.11; N, 18.89.

*(E)-3-Thiol-4-(4-hydroxylbenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5f**)*. White powder, yield: 68.8%, m.p.: 245-246°C. IR (KBr, cm^{-1}): 3129, 3102, 2985, 1611, 1557, 1532, 1483, 1270. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.17 (d, J = 9.0 Hz, 1H, Ar-H), 7.40–7.60 (m, 6H, Ar-H), 7.88–7.90 (m, 2H, Ar-H), 9.49 (s, 1H, CH=N), 10.41 (s, 1H, OH), 14.24 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 115.11, 126.48, 128.21, 128.24, 128.43, 128.85, 130.84, 144.85, 154.74, 159.05, 165.11. Anal. calcd for $C_{15}H_{12}N_4OS$: C, 60.79; H, 4.08; N, 18.91; found: C, 60.73; H, 4.12; N, 19.00.

*(E)-3-Thiol-4-(2-nitrobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5g**)*. Pale yellow needle crystal, yield: 82.1%, m.p.: 214-215°C. IR (KBr, cm^{-1}): 3113, 2974, 1614 1554, 1530, 1482, 1270. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 6.94 (d, J = 8.6 Hz, 2H, Ar-H), 7.49–7.58 (m, 3H, Ar-H), 7.75 (d, J = 8.6 Hz, 2H, Ar-H), 7.86–7.90 (m, 2H, Ar-H), 9.58 (s, 1H, CH=N), 14.32 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 126.45, 127.11, 127.83,. 128.22, 128.25, 128.42, 130.87, 131.67, 133.54, 140.25, 144.83, 146.91, 165.12. Anal. calcd for $C_{15}H_{11}N_5O_2S$: C, 55.38; H, 3.41; N, 21.53; found: C, 55.34; H, 3.46; N, 21.59.

*(E)-3-Thiol-4-(3-nitrobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5h**)*. Pale yellow needle crystal, yield: 72.3%, m.p.: 214-215°C. IR (KBr, cm^{-1}): 3108, 2972, 1620, 1557, 1538, 1487, 1269. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.42 (t, J = 8.8 Hz, 2H, Ar-H), 7.47–7.61 (m, 3H, Ar-H), 7.88 (d, J = 7.6 Hz, 2H, Ar-H), 7.99–8.12 (m, 2H, Ar-H), 9.71 (s, 1H, CH=N), 14.32 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 125.88, 126.76, 128.22, 128.24, 128.44, 129.11, 130.83, 132.97, 135.83, 144.85, 146.87, 155.94, and 165.12. Anal. calcd for $C_{15}H_{11}N_5O_2S$: C, 55.38; H, 3.41; N, 21.53; found: C, 55.42; H, 3.39; N, 21.48.

*(E)-3-Thiol-4-(4-nitrobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5i**)*. Red powder, Yield: 77.6%, m.p.: 238-239°C. IR (KBr, cm^{-1}): 3111, 2971 1610, 1552 1537, 1487, 1269; ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.45–7.72 (m, 6H, Ar-H), 7.82–7.94 (m, 2H, Ar-H), 8.07 (d, J = 7.5 Hz, 1H, Ar-H), 9.55 (s, 1H, CH=N), 14.34 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 123.72, 127.87, 128.23, 128.25, 128.42, 130.86, 138.93, 144.82, 146.85, 154.73, 165.12. Anal. calcd for $C_{15}H_{11}N_5O_2S$: C, 55.38; H, 3.41; N, 21.53; found: C, 55.32; H, 3.45; N, 21.56

*(E)-3-Thiol-4-(2-chlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5j**)*. Pale yellow needle crystal, yield: 73.1%, m.p.: 199-200°C. IR (KBr, cm^{-1}): 3110, 2971, 1614, 1552, 1538, 1483, 1269. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.45–7.63 (m, 3H, Ar-H), 7.80–7.93 (m, 2H, Ar-H), 8.15 (d, J = 8.7 Hz, 2H, Ar-H), 8.38 (d, J = 8.6 Hz, 2H, Ar-H), 9.78 (s, 1H, CH=N), 14.31 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 127.61, 128.21, 128.22, 128.43, 129.07, 129.18, 129.53, 130.43, 130.84, 133.24, 144.86, 150.17, and 165.12. Anal. calcd for

$C_{15}H_{11}ClN_4S$: C, 57.23; H, 3.52; N, 17.80; found: C, 57.28; H, 3.54; N, 17.75.

*(E)-3-Thiol-4-(3-chlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5k**)*. Pale yellow needle crystal, Yield: 69.2%, m.p.: 210-211°C. IR (KBr, cm^{-1}): 3106, 2969, 1618, 1553, 1542, 1488, 1279. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.40–7.61 (m, 3H, Ar-H), 7.78–7.90 (m, 3H, Ar-H), 8.09 (d, J = 8.8 Hz, 1H, Ar-H), 8.38 (d, J = 8.4 Hz, 2H, Ar-H), 9.76 (s, 1H, CH=N), 14.29 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 126.45, 127.48, 128.22, 128.25, 128.42, 129.12, 129.51, 130.85, 134.33, 135.06, 144.84, 155.93, 165.12. Anal. calcd for $C_{15}H_{11}ClN_4S$: C, 57.23; H, 3.52; N, 17.80; found: C, 57.20; H, 3.49; N, 17.76.

*(E)-3-Thiol-4-(4-chlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5l**)*. Pale yellow needle crystal, yield: 68.2%, m.p.: 221-222°C. IR (KBr, cm^{-1}): 3100, 2979, 1611, 1551, 1537, 1481, 1269. ^{1}H NMR (600 MHz, DMSO-*d*6) δ; 7.46–7.68 (m, 5H, Ar-H), 7.85–7.87 (m, 3H, Ar-H), 8.04 (d, J = 8.5 Hz, 1H, Ar-H), 9.78 (s, 1H, CH=N), 14.26 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 128.21, 128.22, 128.41, 128.59, 128.63, 130.85, 134.16, 135.34, 144.85, 154.74, 165.12. Anal. calcd for $C_{15}H_{11}ClN_4S$: C, 57.23; H, 3.52; N, 17.80; found: C, 57.21; H, 3.57; N, 17.77.

*(E)-3-Thiol-4-(2,4-dichlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5m**)*. Pale yellow needle crystal, yield: 69.0%, m.p.: 222-223°C. IR (KBr, cm^{-1}): 3107, 2985, 1620, 1563, 1523, 1481, 1274. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.42 (t, J = 12.1 Hz, 1H, Ar-H), 7.48–7.60 (m, 4H, Ar-H), 7.64–7.67 (m, 1H, Ar-H), 7.92–8.13 (m, 2H, Ar-H), 9.75 (s, 1H, CH=N), 14.31 (s, 1H, triazole–NH). ^{13}C NMR (600 MHz, DMSO-*d*6) δ: 128.21, 128.23, 128.10, 128.22, 128.23, 128.44, 130.86, 132.96, 133.54, 134.96, 144.82, 153.94, 165.13. Anal. calcd for $C_{15}H_{10}Cl_2N_4S$: C, 51.59; H, 2.89; N, 16.04; found: C, 51.53; H, 2.92; N, 16.08.

*(E)-3-Thiol-4-(3,4-dichlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (**5n**)*. White needle crystal, yield: 84.8%, m.p.: 205-206°C. IR (KBr, cm^{-1}): 3112, 2971, 1612, 1554, 1537, 1481, 1275. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 7.39 (d, J = 7.8 Hz, 2H, Ar-H), 7.52–754 (m, 2H, Ar-H), 7.79 (d, J = 7.9 Hz, 2H, Ar-H), 7.84–7.94 (m, 2H, Ar-H), 9.62 (s, 1H, CH=N), 14.29 (s, 1H, triazole–NH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 126.81, 128.04, 128.10, 128.22, 128.26, 128.43, 130.86, 132.95, 133.54, 134.97, 144.84, 155.94, 165.12. Anal. calcd for $C_{15}H_{10}Cl_2N_4S$: C, 51.59; H, 2.89; N, 16.04; found: C, 51.55; H, 2.85; N, 16.01.

*2.6. General Procedure for the Synthesis of Target Compounds (**6a–6n**).* (*E*)-3-Thiol-4-arylideneamino-5-phenyl-4H-1,2,4-triazole **5** (1.75 mmol) was dissolved in DMF (15 mL), and anhydrous potassium carbonate (0.24 g, 1.75 mmol) was added to the solution. The solution was stirred for 0.5 h and (*E*)-methyl-2-(2-(bromomethyl)phenyl)-2-(methoxyimino) acetate (0.50 g, 1.75 mmol) was then added. The reaction mixture was heated to 80°C and monitored by TLC. After 1 h, the mixture was cooled, diluted with water (30 mL), and extracted with ethyl acetate (3 × 100 mL). The combined extracts were washed with brine, dried (anhydrous magnesium sulfate), and filtered. The filtrate was evaporated, and the crude product was purified by silica gel column chromatography using a 1 : 3 (v/v) mixture of ethyl acetate and petroleum ether (boiling point range 60–90°C) as the eluting solution to obtain compound **6**.

*(E)-Methyl-2-(3-((4-((E)-benzylideneamino)-5-phenyl- 4H-1,2,4-triazol-3-ylthio)methyl)phenyl)-2-(methoxyimino)acetate (**6a**)*. White solid, yield: 61.1%, m.p.: 94-95°C. IR (KBr, cm^{-1}): 3103, 2964, 1655, 1611, 1554, 1514, 1478, 1274. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.64 (s, 3H, $COOCH_3$), 3.90 (s, 3H, =N-OCH_3), 4.30 (s, 2H, CH_2), 7.18 (t, J = 15.8 Hz, 1H, Ar-H), 7.31–7.36 (m, 2H, Ar-H), 7.45–7.71 (m, 7H, Ar-H), 7.85–8.14 (m, 4H, Ar-H), 8.74 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.68, 52.18, 60.41, 127.73, 128.16, 128.31, 128.31, 128.34, 128.66, 128.78, 129.47, 130.64, 130.79, 130.93, 131.14, 134.35, 140.63, 149.72, 152.49, 158.56, 159.58, 163.67. ESI-HRMS calcd. for $C_{26}H_{24}N_5O_3S$ $[M + H]^+$ 486.15944; found: 486.15877.

*(E)-Methyl-2-(2-(((4-((E)-(4-methylbenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6b**)*. White solid, yield: 61.2%, m.p.: 119-120°C. IR (KBr, cm^{-1}): 3113, 2963, 1653, 1602, 1567, 1525, 1486, 1285. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 2.97 (s, 3H, Ar-CH_3), 3.65 (s, 3H, $COOCH_3$), 3.90 (s, 3H, =N-OCH_3), 4.29 (s, 2H, CH_2), 7.16 (d, J = 7.5 Hz, 1H, ArH), 7.32–7.41 (m, 4H, Ar-H), 7.46–7.52 (m, 3H, Ar-H), 7.54 (d, J = 7.5 Hz, 1H, Ar-H), 7.76 (d, J = 8.1 Hz, 2H, ArH), 7.81–7.85 (m, 2H, Ar-H), 8.68 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 21.25, 33.71, 52.04, 60.45, 128.04, 128.18, 128.32, 128.33, 128.61, 128.67, 128.74, 130.65, 130.77, 130.93, 131.11, 131.73, 137.93, 140.63, 149.74, 152.49, 158.56, 159.53, 163.50. ESI-HRMS calcd. for $C_{27}H_{26}N_5O_3S$ $[M + H]^+$ 500.17509; found: 500.17536.

*(E)-Methyl-2-(2-(((4-((E)-(4-(dimethylamino)benzylidene) amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6c**)*. White solid, yield: 73.2%, m.p.: 140-141°C. IR (KBr, cm^{-1}): 3105, 2955, 1652, 1612, 1539, 1514, 1491, 1288. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.11 (s, 6H, N-$(CH_3)_2$), 3.67 (s, 3H, $COOCH_3$), 3.91 (s, 3H, =N-OCH_3), 4.26 (s, 2H, CH_2), 6.80 (d, J = 9.0 Hz, 2H, Ar-H), 7.16 (d, J = 7.5 Hz, 1H, Ar-H), 7.33–7.41 (m, 2H, Ar-H), 7.43–7.52 (m, 3H, Ar-H), 7.55 (d, J = 7.4 Hz, 1H, Ar-H), 7.67 (d, J = 8.9 Hz, 2H, Ar-H), 7.84 (d, J = 7.9 Hz, 2H, Ar-H), 8.43 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.71, 41.93, 52.06, 60.44, 111.93, 120.02, 128.15, 128.26, 128.33, 128.34, 128.66, 128.78, 130.61, 130.73, 130.97, 131.19, 140.69, 149.74, 152.46, 153.15, 158.56, 159.53, 163.57. ESI-HRMS calcd. for $C_{28}H_{29}N_6O_3S$ $[M + H]^+$ 529.20164; found: 529.20172.

*(E)-Methyl-2-(2-(((4-((E)-(2-hydroxybenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6d**)*. White solid, yield: 70.2%, m.p.: 117-118°C. IR (KBr, cm^{-1}): 3110, 2952, 1650, 1607, 1541, 1527, 1486, 1282. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.68 (s, 3H, $COOCH_3$), 3.92 (s, 3H, =N-OCH_3), 4.31 (s, 2H, CH_2),

6.96–7.10 (m, 2H, Ar-H), 7.17 (d, J = 7.4 Hz, 1H, Ar-H), 7.31–7.54 (m, 6H, Ar-H), 7.56 (d, J = 7.5 Hz, 2H, Ar-H), 7.83 (d, J = 7.3 Hz, 2H, Ar-H), 8.86 (s, 1H, CH=N), 10.52 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.72, 42.16, 52.03, 60.42, 85.38, 116.27, 119.65, 121.04, 128.17, 128.37, 128.63, 128.71, 129.68, 130.63, 130.77, 130.94, 131.06, 131.13, 140.64, 149.75, 150.16, 152.47, 158.53, 159.94, 163.56. ESI-HRMS calcd. for $C_{26}H_{24}N_5O_4S$ $[M + H]^+$ 502.15435: found: 502.15344.

*(E)-Methyl-2-(2-(((4-((E)-(3-hydroxybenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6e**)*. White solid, yield: 69.3%, m.p.:126-127°C. IR (KBr, cm^{-1}): 3109, 2956, 1651, 1612, 1542, 1523, 1481, 1280. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.68 (s, 3H, $COOCH_3$), 3.92 (s, 3H, =N-OCH_3), 4.31 (s, 2H, CH_2), 6.99 (d, J = 7.5 Hz, 1H, Ar-H), 7.29–7.38 (m, 2H, Ar-H), 7.50–7.52 (m, 5H, Ar-H), 7.61–7.76 (m, 3H, ArH), 7.85 (d, J = 6.4 Hz, 2H, Ar-H), 8.73 (s, 1H, CH=N), 10.50 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.74. 52.05, 60.43, 115.08, 117.21, 120.93, 128.19, 128.29, 128.34, 128.66, 128.78, 130.41, 130.63, 130.76, 130.97, 131.18, 136.93, 140.63, 149.74, 152.47, 157.35, 158.56, 160.02, 163.55. ESI-HRMS calcd. for $C_{26}H_{24}N_5O_4S$ $[M + H]^+$ 502.15435: found: 502.15422.

*(E)-Methyl-2-(2-(((4-((E)-(4-hydroxybenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6f**)*. White solid, yield: 71.0%, m.p.: 143-144°C. IR (KBr, cm^{-1}): 3113, 2953, 1658, 1600, 1546, 1513, 1480, 1278. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.66 (s, 3H, $COOCH_3$), 3.91 (s, 3H, =N-OCH_3), 4.28 (s, 2H, CH_2), 6.94 (d, J = 8.6 Hz, 2H, Ar-H), 7.17 (d, J = 7.5 Hz, 1H, Ar-H), 7.30–7.41 (m, 2H, Ar-H), 7.44–7.52 (m, 3H, Ar-H), 7.55 (d, J = 7.6 Hz, 1H, Ar-H), 7.73 (d, J = 8.7 Hz, 2H, Ar-H), 7.84 (d, J = 8.0 Hz, 2H, Ar-H), 8.55 (s, 1H, CH=N), 10.37 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.72, 52.08, 60.42, 115.12, 126.43, 128.19, 128.35, 128.34, 128.65, 128.78, 128.84, 130.66, 130.77, 130.94, 131.13, 140.65, 149.76, 152.49, 158.56, 159.04, 159.57, 163.56. ESI-HRMS calcd. for $C_{26}H_{24}N_5O_4S$ $[M+H]^+$ 502.15435; found: 502.15425.

*(E)-Methyl-2-(2-(((4-((E)-(2-nitrobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6g**)*. Pale yellow solid, yield: 77.2%, m.p.: 143-144°C. IR (KBr, cm^{-1}): 3112, 2953, 1656, 1612, 1557, 1519, 1493, 1280. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.69 (s, 3H, $COOCH_3$), 3.93 (s, 3H, =N-OCH_3), 4.33 (s, 2H, CH_2), 7.18 (d, J = 7.5 Hz, 1H, Ar-H), 7.33–7.40 (m, 2H, Ar-H), 7.49–7.59 (m, 4H, Ar-H), 7.76–7.83 (m, 2H, Ar-H), 7.84–7.92 (m, 1H, Ar-H), 7.93 (t, J = 17.8 Hz, 1H, Ar-H), 8.04 (d, J = 7.7 Hz, 1H, Ar-H), 8.21 (d, J = 8.1 Hz, 1H, Ar-H), 9.05 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.73, 52.08, 60.40, 126.44, 127.13, 127.80, 128.19, 128.32, 128.33, 128.64, 128.73, 130.65, 130.72, 130.93, 131.13, 131.65, 133.55, 140.64, 146.90, 148.45, 149.75, 152.47, 158.56, 163.58. ESI-HRMS calcd. for $C_{26}H_{23}N_6O_5S$ $[M + H]^+$ 531.14451; found: 531.14424.

*(E)-Methyl-2-(2-(((4-((E)-(3-nitrobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6h**)*. Pale yellow solid, yield: 62.3%, m.p.: 112-113°C. IR (KBr, cm^{-1}): 3105, 2959, 1652, 1609, 1557, 1523, 1482, 1275. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.66 (s, 3H, $COOCH_3$), 3.91 (s, 3H, =N-OCH_3), 4.30 (s, 2H, CH_2), 7.17 (d, J = 7.6 Hz, 1H, Ar-H), 7.30–7.41 (m, 2H, Ar-H), 7.47–7.55 (m, 4H, Ar-H), 7.81–7.92 (m, 3H, Ar-H), 8.31 (d, J = 7.8 Hz, 1H, Ar-H), 8.48 (d, J = 8.2 Hz, 1H, Ar-H), 8.65 (s, 1H, ArH), 8.92 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.71, 52.08, 60.41, 123.87, 124.67, 128.19, 128.35, 128.36, 128.65, 128.78, 129.10, 130.65, 130.74, 130.93, 131.13, 132.97, 135.86, 140.63, 146.85, 149.75, 152.46, 158.54, 160.05, 163.56. ESI-HRMS calcd. for $C_{26}H_{23}N_6O_5S$ $[M + H]^+$ 531.14451; found: 531.14415.

*(E)-Methyl-2-(2-(((4-((E)-(4-nitrobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6i**)*. Yellow solid, yield: 78.5%, m.p.: 140-141°C. IR (KBr, cm^{-1}): 3103, 2957, 1648, 1614, 1567, 1528, 1491, 1273. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.65 (s, 3H, $COOCH_3$), 3.91 (s, 3H, =N-OCH_3), 4.31 (s, 2H, CH_2), 7.16 (d, J = 7.5 Hz, 1H, Ar-H), 7.31–7.40 (m, 2H, Ar-H), 7.45–7.58 (m, 4H, Ar-H), 7.82 (d, J = 9.5, 2H, Ar-H), 8.12 (d, J = 8.8 Hz, 2H, Ar-H), 8.40 (d, J = 8.8 Hz, 2H, Ar-H), 8.89 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.71, 52.08, 60.42, 123.73, 127.85, 128.18, 128.36, 128.34, 128.66, 128.78, 130.66, 130.79, 130.93, 131.13, 138.94, 140.63, 146.84, 149.75, 152.49, 158.56, 159.58, 163.58. ESI-HRMS calcd. for $C_{26}H_{23}N_6O_5S$ $[M + H]^+$ 531.14451; found: 531.14434.

*(E)-Methyl-2-(2-(((4-((E)-(2-chlorobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6j**)*. Pale yellow solid, yield: 63.2%, m.p.: 122-123°C. IR (KBr, cm^{-1}): 3122, 2956, 1650, 1612, 1557, 1524, 1498, 1281. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.67 (s, 3H, $COOCH_3$), 3.92 (s, 3H, =N-OCH_3), 4.34 (s, 2H, CH_2), 7.09–7.21 (m, 1H, Ar-H), 7.33–7.40 (m, 2H, Ar-H), 7.48–7.71 (m, 7H, Ar-H), 7.82 (d, J = 7.5, 2H, Ar-H), 8.05 (d, J = 7.5 Hz, 1H), 8.95 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.71, 52.08, 60.41, 127.68, 128.14, 128.32, 128.35, 128.66, 128.78, 129.07, 129.14, 129.52, 130.43, 130.65, 130.77, 130.95, 131.13, 133.23, 140.63, 149.75, 152.48, 155.05, 158.54, 163.56. ESI-HRMS calcd. for $C_{26}H_{23}ClN_5O_3S$ $[M + H]^+$ 520.12046; found: 520.12032.

*(E)-Methyl-2-(2-(((4-((E)-(3-chlorobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6k**)*. Pale yellow solid, yield: 60.9%, m.p.: 126-127°C. IR (KBr, cm^{-1}): 3117, 2961, 1652, 1623, 1555, 1529, 1492, 1284. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.63 (s, 3H, $COOCH_3$), 3.89 (s, 3H, =N-OCH_3), 4.32 (s, 2H, CH_2), 7.17 (d, J = 7.4 Hz, 1H, Ar-H), 7.30–7.41 (m, 2H, Ar-H), 7.46–7.57 (m, 5H, Ar-H), 7.75–7.82 (m, 2H, Ar-H), 7.92 (d, J = 7.5 Hz, 2H, Ar-H), 8.05 (s, 1H, Ar-H), 8.85 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.72, 52.05, 60.44, 126.43, 127.44, 128.18, 128.31, 128.33, 128.66, 128.78, 129.13, 129.51, 130.65, 130.77, 130.98, 131.12, 134.32, 135.05, 140.62, 149.75, 152.49, 158.56, 160.02, 163.56. ESI-HRMS calcd. for $C_{26}H_{23}ClN_5O_3S$ $[M + H]^+$ 520.12046; found: 520.12031.

Table 1: Fungicidal activities of **6a–6n** (inhibition rate/%, 50 μg mL^{-1}).

Entry	*Rhizoctonia solani*	*Botrytis cinerea Pers.*	*Fusarium graminearum*	*Cotton rhizoctoniosis*	*Blumeria graminis*
6a	26.87	12.73	17.13	17.03	37.13
6b	15.37	20.91	15.31	15.23	33.49
6c	13.43	13.64	8.67	9.31	91.41
6d	21.94	43.64	18.78	19.43	25.31
6e	18.32	40.21	15.45	18.69	31.60
6f	17.46	22.73	11.13	19.34	43.49
6g	48.96	62.73	60.13	25.31	37.13
6h	26.45	39.09	23.49	23.49	13.02
6i	11.94	19.09	12.36	10.00	82.63
6j	47.91	60.45	59.54	19.67	33.49
6k	35.65	45.31	38.64	17.98	45.46
6l	17.91	16.36	12.76	17.13	92.13
6m	27.91	37.27	11.67	11.49	91.77
6n	27.46	22.73	17.13	12.31	43.49
Kresoxim-methyl	65.32	81.69	73.36	61.56	100

*(E)-Methyl-2-(2-(((4-((E)-(4-chlorobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6l**)*. Pale yellow solid, yield: 70.1%, m.p.: 131-132°C. IR (KBr, cm^{-1}): 3112, 2952, 1654, 1601, 1552, 1522, 1479, 12820. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.65 (s, 3H, $COOCH_3$), 3.90 (s, 3H, =N-OCH_3), 4.29 (s, 2H, CH_2), 7.17 (d, J = 6.9 Hz, 1H, Ar-H), 7.30–7.54 (m, 6H, Ar-H) 7.66 (d, J = 7.6 Hz, 2H, Ar-H), 7.82 (d, J = 4.8 Hz, 2H, Ar-H), 7.89 (d, J = 7.7 Hz, 2H, Ar-H), 8.75 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.44. 52.97, 61.75, 126.74, 128.09, 128.28, 129.07, 129.30, 129.89, 130.01, 130.52, 130.68, 130.96, 131.17, 135.09, 138.63, 146.80, 149.10, 151.63, 158.01, 159.56, 163.69. ESI-HRMS calcd. for $C_{26}H_{23}ClN_5O_3S$ $[M + H]^+$ 520.12046; found: 520.11952.

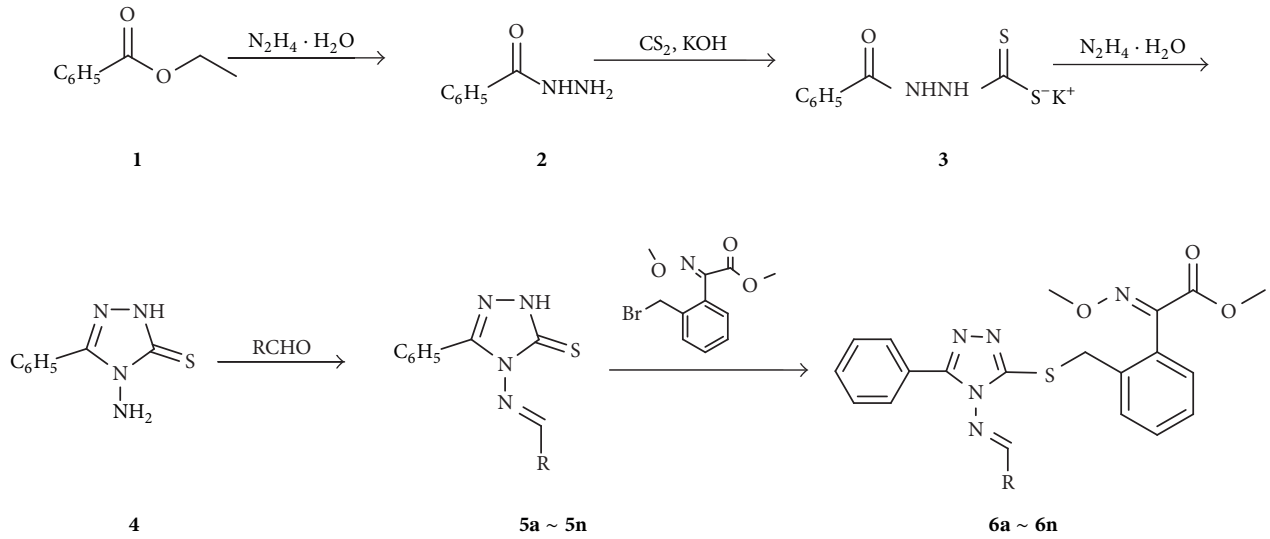
*(E)-Methyl-2-(2-(((4-((E)-(2,4-dichlorobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6m**)*. Pale yellow solid, yield: 71.6%, m.p.: 142-143°C. IR (KBr, cm^{-1}): 3099, 2967, 1646, 1609, 1561, 1514, 1488, 1278. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.68 (s, 3H, $COOCH_3$), 3.92 (s, 3H, =N-OCH_3), 4.33 (s, 2H, CH_2), 7.17 (d, J = 7.4 Hz, 1H, Ar-H), 7.32–7.38 (m, 2H, Ar-H), 7.49–7.59 (m, 4H, Ar-H), 7.63 (d, J = 8.5 Hz, 1H, Ar-H), 7.80 (d, J = 4.4 Hz, 2H, Ar-H), 7.86 (s, 1H, Ar-H), 8.03 (d, J = 8.5 Hz, 1H, Ar-H), 8.90 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.72, 52.08, 60.30, 128.29, 128.34, 128.36, 128.38, 128.66, 128.68, 129.58, 129.75, 129.96, 130.65, 130.77, 130.97, 131.14, 134.57, 134.72, 140.63, 149.75, 152.48, 155.09, 158.57, 163.57. ESI-HRMS calcd. for $C_{26}H_{22}C_{l2}N_5O_3S$ $[M + H]^+$ 554.08149; found: 554.08127.

*(E)-Methyl-2-(2-(((4-((E)-(3,4-dichlorobenzylidene)amino)-5-phenyl-4H-1,2,4-triazol-3-yl)thio)methyl)phenyl)-2-(methoxyimino)acetate (**6n**)*. Pale yellow solid, yield: 74.6%, m.p.: 101-102°C. IR (KBr, cm^{-1}): 3111, 2957, 1655, 1601, 1547, 1530, 1498, 1279. ^{1}H NMR (600 MHz, DMSO-*d*6) δ: 3.58 (s, 3H, $COOCH_3$), 3.91 (s, 3H, =N-OCH_3), 4.29 (s, 2H, CH_2), 7.17 (d, J = 7.4 Hz, 1H, Ar-H), 7.31–7.40 (m, 2H, Ar-H), 7.46–7.55 (m, 4H, Ar-H), 7.81–7.84 (m, 2H, Ar-H), 7.85 (d, J = 9.2 Hz, 2H, Ar-H), 8.09 (s, 1H, Ar-H), 8.75 (s, 1H, CH=N). ^{13}C NMR (125 MHz, DMSO-*d*6) δ: 33.71, 52.06, 60.31, 128.29, 128.32, 128.33, 128.38, 128.66, 128.66, 129.58, 129.75, 129.97, 130.65, 130.76, 130.97, 131.15, 134.57, 134.73, 140.63, 149.74, 152.48, 155.08, 158.57, 163.56. ESI-HRMS calcd. for $C_{26}H_{22}Cl_2N_5O_3S$ $[M + H]^+$ 554.08149; found: 554.08121.

2.7. Antimicrobial Activity Assessment. Inhibitive, active freshly prepared compounds were tested by mycelium growth rate method under the laboratory conditions, and these strobilurin derivatives were screened for antifungal activity against *Rhizoctonia solani*, *Botrytis cinerea Pers.*, *Fusarium graminearum*, *Cotton rhizoctoniosis,* and *Blumeria graminis* at dosages of 50 μg mL^{-1}. Antifungal activity was determined by measuring the diameter of the inhibition zone. The growth inhibition rates were calculated by using the following equation: $I = [(C - T)/C] \times 100\%$. Here, I is the growth inhibition rate (%), C is the control settlement radius (mm), and T is the treatment group fungi settlement radius (mm). Activity of each compound was compared to kresoxim-methyl as standard. The results of preliminary screening are listed in Table 1.

3. Results and Discussion

3.1. Synthetic Chemistry. Scheme 1 shows the schematic representation of the synthetic route for the preparation of target compounds. Compound **2** was prepared by the reaction between ethyl benzoate **1** and 85% hydrazine hydrate in ethanol at room temperature in excellent yield (90.6%). Further, compound **2** was heated with carbon disulfide in



Scheme 1: Synthetic route of target compounds **6a**–**6n**. **R** =: **6a**. C_6H_5; **6b**. 4-$CH_3C_6H_4$; **6c**. 4-$N(CH_3)_2C_6H_4$; **6d**. 2-OHC_6H_4; **6e**. 3-OHC_6H_4; **6f**. 4-OHC_6H_4; **6g**. 2-$NO_2C_6H_4$; **6h**. 3-$NO_2C_6H_4$; **6i**. 4-$NO_2C_6H_4$; **6j**. 2-ClC_6H_4; **6k**. 3-ClC_6H_4; **6l.** 4-ClC_6H_4; **6m**. 2, 4-$Cl_2C_6H_3$; **6n**. 3,4-$Cl_2C_6H_3$.

the presence of absolute ethanol and potassium hydroxide to afford intermediate potassium acylhydrazine dithioformate **3**. This salt underwent ring closure with an excess of 85% hydrazine hydrate to give intermediate **4**, which was used directly without further purification for the subsequent reaction. Subsequently, compound **4** was allowed to react with appropriate aromatic aldehydes and 2 to 3 drops of glacial acetic acid to produce series of compounds **5** in moderate yield according to the method reported in the literature [18]. Finally, a series of the target compounds **6** were obtained by the reaction of corresponding compounds **5** with (*E*)-methyl-2-(2-(bromomethyl)phenyl)-2-(methoxyimino)acetate in the presence of base following the literature method [26]. The structures of the desired compounds were confirmed by ^{1}H NMR, ^{13}C NMR, IR, and ESI-HRMS.

3.2. Biological Evaluation. The fungicidal activities of the series of title compounds **6** were tested at a concentration of 50 μg mL^{-1} by a modified method described in the literature [27]. The five fungi used in the fungicidal bioassay, *Rhizoctonia solani*, *Botrytis cinerea Pers.*, *Fusarium graminearum*, *Cotton rhizoctoniosis*, and *Blumeria graminis*, were tested by mycelium growth rate method. The commercial agricultural fungicide kresoxim-methyl was used as a standard.The results of preliminary bioassays are listed in Table 1.

The values listed in Table 1 clearly indicate that all the compounds do not exhibit good fungicidal activity against *Cotton rhizoctoniosis* at the concentration of 50 μg mL^{-1}. However, the compounds **6g** and **6j** exhibited promising antifungal activity, inhibiting growth of *Rhizoctonia solani* at 48.96% and 47.91%, *Botrytis cinerea Pers.* at 62.73% and 60.45%, and *Fusarium graminearum* at 60.13% and 59.54%, respectively. However, the obtained values were still less than that of kresoxim-methyl (65.32% against *Rhizoctonia solani*, 81.69% against *Botrytis cinerea Pers.*, and 73.36% against *Fusarium graminearum* at 50 μg mL^{-1}). Moreover, compounds **6c**, **6l**, and **6m** exhibited 91.41, 92.13, and 91.77% inhibitory activity against *Blumeria graminis*, respectively.

Interestingly, the fungicidal activities of the synthesized compounds **6** were influenced by the position of substituted group on the benzene ring. The sequence of fungicidal activity against *Rhizoctonia solani*, *Botrytis cinerea Pers.*, and *Fusarium graminearum* was as follows: *o*-substituted-benzylidene derivatives > *m*-substituted-benzylidene derivatives > *p*-substituted- benzylidene derivatives. Surprisingly, for the *p*-substituted benzylidene, the fungicidal activity against *Blumeria graminis* was significantly enhanced.

4. Conclusion

A series of novel (*E*)-α-methoxyimino-benzeneacetate derivatives were synthesized. They were characterized by IR, ^{1}H NMR, ^{13}C NMR, and ESI-HRMS. All the synthesized compounds were screened for their antifungal activity by mycelium growth rate method. The antifungal tests indicated that compounds **6g** and **6j** exhibited promising antifungal activity against *Rhizoctonia solani*, *Botrytis cinerea Pers.*, and *Fusarium graminearum*. Moreover, compounds **6c**, **6l**, and **6m** exhibited higher fungicidal activities against *Blumeria graminis*. Therefore, this study demonstrated that methoxyiminoacetate derivatives containing 1,2,4-triazole Schiff base side chain acted as promising candidates for developing novel fungicides. This study provides an impetus to the further exploration of antifungal compounds. Further research involving design, synthesis, and structure optimizations is still in progress.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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