Synthesis and Antifungal Activities of Some Novel 1,2,4-Triazole Derivatives

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To find new 1,2,4-triazole derivatives which may possess significant biological activities, we synthesized a series of Schiff bases bearing 1,2,4-triazole ring derivatives. Their structures were confirmed by elemental analysis, IR, ¹H NMR. The biological activity tests showed that some of the target compounds showed certain fungicidal activities against *Gibberella zeae*, *Phytophthora infestans*, *Botrytis cinerea* at dosages of 50 µg/mL.

Keywords: 1,2,4-Triazole, Schiff base, Synthesis, Antifungal activity.

INTRODUCTION

Currently, nitrogen containing heterocyclic compounds has received considerable attention due to their wide range of bioactivity activities¹⁻³. Especially, various substituted 1,2,4-triazolo and Schiff's bases are associated with diverse biological activities, such as pesticides, fungicides, herbicidal, anticancer, antiinflammatory, antiviral and antimicrobial properties⁴⁻⁸.

As the most important part of pesticide, the triazole fungicide is developed more wide varieties than other pesticides, because the triazole compounds have power aspiration, lower toxicities and shorter residual effects. Triazol compounds of different structures have different biological activity and developing new type of the compound becomes are search focus at present.

In order to find highly active fungicide, the different substituted moieties of benzaldehyde derivatives were introduced into 1,2,4-triazolo matrix structure according to the law of biological electron row principle and active substructure connection in this paper. We now report the synthesis of 22 compounds containing 1,2,4-triazolo and Schiff's bases. The target compounds were prepared following the reaction sequences depicted in **Scheme-I**.

EXPERIMENTAL

All melting points were determined on an XT-4A apparatus and are uncorrected. The IR spectra (KBr disks) were taken on a Bruker Quinox 55 spectrophotometer. The ¹H NMR spectra were measured on a Bruker Advance 600 spectrometer for DMSO-*d*₆ solutions using TMS as internal standard. Elemental analyses were determined on a Flash-1112 series

elemental analyzer. All the reagents used were AR grade. The completion of reactions was monitored by TLC.

Synthesis of 4-amino-3-phenyl-5-thiol-1,2,4-triazole (4)⁹: Ethyl benzoate **1** (30 mL) and 85 % hydrazine hydrate (15 mL) were converted first to the corresponding benzohydrazide **2**. benzohydrazide **2** (0.1 mol) was heated with carbon disulfide (10 mL) in the presence of absolute ethanol (100 mL) and potassium hydroxide (10 g) to afford intermediate potassium acylhydrazine dithioformate **3** (**Scheme-I**). This salt (0.05 mol) underwent ring closure with an excess of 85 % hydrazine hydrate (0.15 mol) 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, $\nu_{\max}$, cm⁻¹): 3412, 3070, 2667, 1640; ¹H NMR (600 MHz, DMSO-*d*₆) δ : 13.90 (s, 1H, triazole-NH), 7.52-8.01 (m, 5H, Ar-H), 5.81 (s, 2H, NH₂).

General method for the preparation of (E)-3-thiol-4-arylideneamino-5-phenyl-4H-1,2,4-triazole (5a-5v): To a solution of compound **4** (10 mmol) dissolved in absolute alcohol (30 mL), the appropriate benzaldehyde (10 mmol) and 2 to 3 drops of glacial acetic acid were added. The mixture was refluxed for 4 h with stirring. The solid that was obtained upon cooling was filtered, washed with cold water, dried and recrystallized from alcohol to give the Schiff bases **5a-5v**.

(E)-3-Thiol-4-benzylideneamino-5-phenyl-4H-1,2,4-triazole (5a): White powder, Yield: 70 %, m.p.: 180-181 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3102 (ArH), 2974, 1610, 1554, 1530 (CH₃), 1482 (C=N, C=C), 1269 (C=S); ¹H 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). Anal. Calcd for C₁₅H₁₂N₄S; C, 64.26; H, 4.31; N, 19.98; Found: C, 64.31; H, 4.29; N, 19.93.

Scheme-I: R=: 5a. C₆H₅; 5b. 4-CH₃OC₆H₄; 5c. 4-CH₃C₆H₄; 5d. 4-ClC₆H₄; 5e. 4-BrC₆H₄; 5f. 4-FC₆H₄; 5g. 4-OHC₆H₄; 5h. 4-N(CH₃)₂C₆H₃; 5i. 4-NO₂C₆H₄; 5j. 2-NO₂C₆H₄; 5k. 3-NO₂C₆H₄; 5l. 2,4-Cl₂C₆H₃; 5m. 3,4-(OCH₃)₂C₆H₃; 5n. 2-OCH₃C₆H₄; 5o. 2-ClC₆H₄; 5p. 2-Cl-6-FC₆H₃; 5q. 2-FC₆H₄; 5r. 3,4-Cl₂C₆H₃; 5s. 2-BrC₆H₄; 5t. 3-BrC₆H₄; 5u. 2-OHC₆H₄; 5v. 3-FC₆H₄. i. (1) N₂H₄·H₂O, EtOH; ii. CS₂, KOH, EtOH; iii. N₂H₄·H₂O, EtOH, reflux; iv. RCHO, EtOH, CH₃COOH

(E)-3-Thiol-4-(4-methoxybenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5b): White crystal, Yield: 71.5 %, m.p.: 205–206 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3106 (ArH), 2974, 1634, 1524, 1520 (CH₃), 1487 (C=N, C=C), 1273 (C=S); ¹H NMR (600 MHz, DMSO-*d*₆) δ : 3.86 (s, 3H, OCH₃), 7.12 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.53 (d, *J* = 6.0 Hz, 3H, Ar-H), 7.81–7.94 (m, 4H, Ar-H), 9.50 (s, 1H, CH=N), 14.27 (s, 1H, triazole-NH). Anal. Calcd for C₁₆H₁₄N₄OS; C, 61.92; H, 4.55; N, 18.05; Found: C, 61.97; H, 4.53; N, 18.03.

(E)-3-Thiol-4-(4-methylbenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5c): Red solid, Yield: 62.5 %, m.p.: 239–240 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3110 (ArH), 2979, 1618, 1516, 1512 (CH₃), 1484 (C=N, C=C), 1271 (C=S); ¹H NMR (600 MHz, DMSO-*d*₆) δ : 2.41 (s, 3H, CH₃), 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). Anal. Calcd for C₁₆H₁₄N₄S; C, 65.28; H, 4.79; N, 19.03; Found: C, 65.33; H, 4.77; N, 18.99.

(E)-3-Thiol-4-(4-chlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5d): Pale yellow needle crystal, Yield: 68.2 %, m.p.: 221–222 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3100 (ArH), 2979, 1611, 1551, 1537 (CH₃), 1481 (C=N, C=C), 1269 (C=S); ¹H 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). Anal. Calcd for C₁₅H₁₁N₄SCl; C, 57.23; H, 3.52; N, 17.80; Found: C, 57.21; H, 3.57; N, 17.77.

(E)-3-Thiol-4-(4-bromobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5e): Pale yellow needle crystal, Yield: 67.8 %, m.p.: 226–227 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3114 (ArH), 2977, 1614, 1554, 1531 (CH₃), 1481 (C=N, C=C), 1275 (C=S); ¹H NMR (600 MHz, DMSO-*d*₆) δ : 7.43–7.63 (m, 3H, Ar-H), 7.81–7.94 (m, 4H, Ar-H), 7.79 (d, *J* = 8.4 Hz, 2H, Ar-H), 9.77 (s, 1H, CH=N), 14.26 (s, 1H, triazole-NH). Anal. Calcd for C₁₅H₁₁N₄SB; C, 50.15; H, 3.09; N, 15.60; Found: C, 50.21; H, 3.04; N, 15.56.

(E)-3-Thiol-4-(4-fluorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5f): White crystal, Yield: 64.6 %, m.p.: 172–173 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3112 (ArH), 2970, 1614, 1522, 1512 (CH₃), 1487 (C=N, C=C), 1274 (C=S); ¹H NMR (600

MHz, DMSO-*d*₆) ¹H NMR (600 MHz, DMSO) δ : 6.81 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.52 (s, 3H, Ar-H), 7.70 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.81–7.94 (m, 2H, Ar-H), 9.50 (s, 1H, CH=N), 14.24 (s, 1H, triazole-NH). Anal. Calcd for C₁₅H₁₁N₄SF; C, 60.39; H, 3.72; N, 18.78; Found: C, 60.44; H, 3.69; N, 18.70.

(E)-3-Thiol-4-(4-hydroxybenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5g): White powder, Yield: 68.8 %, m.p.: 245–246 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3129 (OH), 3102 (ArH), 2985, 1611, 1557, 1532 (CH₃), 1483 (C=N, C=C), 1270 (C=S); ¹H 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). Anal. Calcd for C₁₅H₁₂N₄OS; C, 60.79; H, 4.08; N, 18.91; Found: C, 60.73; H, 4.12; N, 19.00.

(E)-3-Thiol-4-(4-dimethylaminobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5h): White solid, Yield: 75.1 %, m.p.: 233–234 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3113 (ArH), 2978, 1613 1552 1531 (CH₃), 1482 (C=N, C=C), 1275 (C=S); ¹H NMR (600 MHz, DMSO-*d*₆) δ : 3.34 (s, 6H, N-(CH₃)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). Anal. Calcd for C₁₇H₁₇N₅S; C, 63.13; H, 5.30; N, 21.65; Found: C, 63.20; H, 5.26; N, 21.59.

(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, $\nu_{\max}$, cm⁻¹): 3111 (ArH), 2971, 1610, 1552 1537 (CH₃), 1487 (C=N, C=C), 1269 (C=S); ¹H 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). Anal. Calcd for C₁₅H₁₁N₅O₂S; C, 55.38; H, 3.41; N, 21.53; Found: C, 55.32; H, 3.45; N, 21.56.

(E)-3-Thiol-4-(2-nitrobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5j): Pale yellow needle crystal, Yield: 82.1 %, m.p.: 214–215 °C ; IR: (KBr, $\nu_{\max}$, cm⁻¹): 3113 (ArH), 2974, 1614 1554, 1530 (CH₃), 1482 (C=N, C=C), 1270 (C=S); ¹H 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). Anal. Calcd for C₁₅H₁₁N₅O₂S; 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 (5k): Pale yellow needle crystal, Yield: 72.3 %, m.p.: 214-215 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3108 (ArH), 2972, 1620, 1557, 1538 (CH_3), 1487 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1269 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) 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 (dd, $J = 8.5, 5.7$ Hz, 2H, Ar-H), 9.71 (s, 1H, $\text{CH}=\text{N}$), 14.32 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_5\text{O}_2\text{S}$; C, 55.38; H, 3.41; N, 21.53; Found: C, 55.42; H, 3.39; N, 21.48.

(E)-3-thiol-4-(2,4-dichlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5l): Pale yellow needle crystal, Yield: 69.0 %, m.p.: 222-223 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3107 (ArH), 2985, 1620, 1563, 1523 (CH_3), 1481 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1274 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) 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 (dd, $J = 15.3, 13.8$ Hz, 2H, Ar-H), 9.75 (s, 1H, $\text{CH}=\text{N}$), 14.31 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{N}_4\text{SCl}_2$; 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-dimethoxybenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5m): White needle crystal, Yield: 71.2 %, m.p.: 199-201 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3100 (ArH), 2971, 1610, 1545, 1535 (CH_3), 1487 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1273 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 3.83 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 7.47-7.65 (m, 2H, Ar-H), 7.99-7.81 (m, 4H, Ar-H), 8.10 (d, $J = 7.5$ Hz, 1H, Ar-H), 8.20 (d, $J = 7.8$ Hz, 1H, Ar-H), 9.52 (s, 1H, $\text{CH}=\text{N}$), 14.28 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_4\text{O}_2\text{S}$; C, 59.98; H, 4.74; N, 16.40; Found: C, 60.01; H, 4.79; N, 16.41.

(E)-3-Thiol-4-(2-methoxybenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5n): White solid, m = 2.15 g, Yield: 69.4 %, m.p.: 206-207 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3116 (ArH), 2980, 1623, 1565, 1520 (CH_3), 1487 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1274 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 3.90 (s, 3H, OCH_3), 7.34-7.67 (m, 3H, Ar-H), 7.87 (dd, $J = 9.6, 7.8$ Hz, 3H, Ar-H), 8.35 (d, $J = 7.7$ Hz, 1H, Ar-H), 8.46 (d, $J = 7.9$ Hz, 1H, Ar-H), 8.67 (s, 1H, Ar-H), 9.73 (s, 1H, $\text{CH}=\text{N}$), 14.29 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{N}_4\text{OS}$; C, 61.92; H, 4.55; N, 18.05; Found: C, 61.89; H, 4.59; N, 18.10.

(E)-3-Thiol-4-(2-chlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5o): Pale yellow needle crystal, Yield: 73.1 %, m.p.: 199-200 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3110 (ArH), 2971, 1614, 1552, 1538 (CH_3), 1483 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1269 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.45-7.63 (m, 3H), 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, $\text{CH}=\text{N}$), 14.31 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_4\text{SCl}$; C, 57.23; H, 3.52; N, 17.80; Found: C, 57.28; H, 3.54; N, 17.75.

(E)-3-Thiol-4-(2-chloro-6-fluorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5p): White needle crystal, Yield: 80.9 %, m.p.: 200-201 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3116 (ArH), 2970, 1610, 1532, 1520 (CH_3), 1481 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1275 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.40-7.42 (m, 2H, Ar-H), 7.50-7.59 (m, 3H, Ar-H), 7.70-7.72 (m, 1H, Ar-H), 7.85-7.92 (m, 2H, Ar-H), 8.00 (t, $J = 7.1$ Hz, 1H, Ar-H), 9.74 (s, 1H, $\text{CH}=\text{N}$), 14.31 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{N}_4\text{SClF}$; C, 54.14; H, 3.03; N, 16.84; Found: C, 54.15; H, 3.04; N, 16.78.

(E)-3-Thiol-4-(2-fluorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5q): White needle crystal, Yield: 72 %, m.p.: 178-179 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3113 (ArH), 2982, 1612, 1553, 1535 (CH_3), 1481 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1272 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.55-7.57 (m, 3H, Ar-H), 7.74-7.96 (m, 5H, Ar-H), 8.09-8.11 (m, 1H, Ar-H), 9.76 (s, 1H, $\text{CH}=\text{N}$), 14.28 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_4\text{SF}$; C, 60.39; H, 3.72; N, 18.78; Found: C, 60.34; H, 3.76; N, 18.80.

(E)-3-Thiol-4-(3,4-dichlorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5r): White needle crystal, Yield: 84.8 %, m.p.: 205-206 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3112 (ArH), 2971, 1612, 1554, 1537 (CH_3), 1481 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1275 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.39 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.52-7.54 (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, $\text{CH}=\text{N}$), 14.29 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{N}_4\text{SCl}_2$; C, 51.59; H, 2.89; N, 16.04; Found: C, 51.55; H, 2.85; N, 16.01.

(E)-3-Thiol-4-(2-bromobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5s): Pale yellow needle crystal, Yield: 72.3 %, m.p.: 181-182 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3102 (ArH), 2975, 1614, 1555, 1537 (CH_3), 1487 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1272 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.53-7.56 (m, 5H, Ar-H), 7.76-7.92 (m, 3H, Ar-H), 8.03-8.05 (m, 1H, Ar-H), 9.63 (s, 1H, $\text{CH}=\text{N}$), 14.36 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_4\text{SBr}$; C, 50.15; H, 3.09; N, 15.60; Found: C, 50.12; H, 3.06; N, 15.62.

(E)-3-Thiol-4-(3-bromobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5t): White needle crystal, Yield: 71.8 %, m.p.: 190-191 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3103 (ArH), 2973, 1620, 1551, 1530 (CH_3), 1487 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1274 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.44-7.64 (m, 4H, Ar-H), 7.75-7.94 (m, 4H, Ar-H), 8.02 (s, 1H, Ar-H), 9.78 (s, 1H, $\text{CH}=\text{N}$), 14.32 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_4\text{SBr}$; C, 50.15; H, 3.09; N, 15.60; Found: C, 50.19; H, 3.10; N, 15.56.

(E)-3-Thiol-4-(2-hydroxybenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5u): White needle crystal, Yield: 78.4 %, m.p.: 195-196 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3122 (OH), 3102 (ArH), 2977, 1620, 1550, 1531 (CH_3), 1486 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1269 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) 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), 7.73-7.93 (m, 3H, Ar-H), 9.65 (s, 1H, $\text{CH}=\text{N}$), 10.47 (s, 1H, Ar-OH), 14.21 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{12}\text{N}_4\text{OS}$; C, 60.79; H, 4.08; N, 18.91; Found: C, 60.73; H, 4.10; N, 18.94.

(E)-3-Thiol-4-(3-fluorobenzylideneamino)-5-phenyl-4H-1,2,4-triazole (5v): White needle crystal, Yield: 70 %, m.p.: 171-172 °C ; IR: (KBr, $\nu_{\max}$, cm^{-1}): 3114 (ArH), 2971, 1612, 1558, 1535 (CH_3), 1482 ($\text{C}=\text{N}$, $\text{C}=\text{C}$), 1270 ($\text{C}=\text{S}$); ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 7.46-7.73 (m, 5H, Ar-H), 7.71-7.74 (m, 2H, Ar-H), 7.84-7.92 (m, 2H, Ar-H), 9.62 (s, 1H, $\text{CH}=\text{N}$), 14.28 (s, 1H, triazole-NH). Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{N}_4\text{SF}$; C, 60.39; H, 3.72; N, 18.78; Found: C, 60.42; H, 3.70; N, 18.76.

Antifungal activities: Under the condition of laboratory, inhibitive active of newly prepared compounds were tested by means of mycelium growth rate method¹⁰. All these 1,2,4-triazole derivatives were screened for antifungal activity against *Gibberella zeae*, *Phytophthora infestans*, *Botrytis cinerea* at dosages of 50 $\mu\text{g/mL}$. Antifungal activity was determined by measuring the diameter of the inhibition zone. Activity of each compound was compared with tradimefon as standard. The results of preliminary screening are summarized in Table-1.

RESULTS AND DISCUSSION

Synthetic Chemistry: According to procedures exemplified above, containing 1,2,4-triazole Schiff base derivatives were synthesized mostly with good overall yields of 62.5–84.8 %. The synthesized compounds were characterized by ^1H NMR, IR and elemental analyses. All spectral and analytical data were consistent with the assigned structures.

The IR spectra of the 3-thiol-4- substituted benzylidene-amino-5-phenyl-1,2,4-triazole (**5a-5v**) showed two characteristic absorption bands, one of which appearing at $1487\text{--}1481\text{ cm}^{-1}$, was attributed to $\text{C}=\text{N}$ or $\text{C}=\text{C}$ and the other at $1275\text{--}1269\text{ cm}^{-1}$, was assigned to $\text{C}=\text{S}$. The ^1H NMR spectrum of compounds **5** showed multiplet at $\delta 6.81\text{--}8.46$ was due to aromatic ring protons, a singlet at $\delta 9.49\text{--}9.78$ corresponds to $\text{CH}=\text{N}$ proton. Similarly a singlet at $14.21\text{--}14.36$ was due to triazole-NH proton, respectively.

Biological evaluation: The three fungi used in the fungicidal bioassay, *Gibberella zeae*, *Phytophthora infestans* and *Botrytis cinerea*, were tested by using mycelium growth rate method. The results of preliminary bioassays were compared with that of a commercial agricultural fungicide, tradimefon (Table-1).

TABLE- 1
FUNGICIDAL ACTIVITIES OF **5a-5v**
[INHIBITION RATE (%), 50 $\mu\text{g/mL}$]

Entry	<i>Gibberella zeae</i>	<i>Phytophthora infestans</i>	<i>Botrytis cinerea</i>
5a	30.2	26.0	15.1
5b	20.1	32.2	14.2
5c	26.4	33.4	12.8
5d	29.5	24.8	18.2
5e	32.5	26.0	24.3
5f	34.3	32.2	22.0
5g	17.1	16.1	12.7
5h	38.2	31.0	23.9
5i	22.4	18.7	23.1
5j	24.1	21.4	25.2
5k	28.4	25.8	26.8
5l	23.9	27.2	18.5
5m	26.3	23.1	13.2
5n	20.0	18.7	19.6
5o	41.2	32.2	22.1
5p	40.6	29.1	21.0
5q	47.5	38.3	29.7
5r	28.8	25.5	24.3
5s	44.2	31.8	27.2
5t	55.3	61.1	49.0
5u	28.8	17.0	13.4
5v	62.0	66.2	58.6
Tradimefon	71.3	76.8	68.2

The new compounds **5t** and **5v** exhibited promising antifungal activity, inhibiting growth of *Gibberella zeae* at 55.3 and 62 %, *Phytophthora infestans* at 61.1 and 66.2 % and *Botrytis cinerea* at 49 and 58.6 %, respectively. But which is still less than that of tradimefon (71.3 % against *Gibberella zeae*, 76.8 % against *Phytophthora infestans* and 68.2 % against *Botrytis cinerea* at 50 $\mu\text{g/mL}$). Marked loss of activity was observed with other compounds such as **5a-5s** and **5u**.

Although it seems impossible to extract an obvious structure-activity relationship from the data shown in Table-1. These results also demonstrated that the introduction of fluorine or bromine substituted benzene rings to the 1,2,4-triazole might improve their fungicidal activities. On the other hand, halogen atoms substituted position based on the benzene ring also has a great influence on the antibacterial activity and overall, the sequence of fungicidal activity against *Gibberella zeae*, *Phytophthora infestans* and *Botrytis cinerea* is *m*-fluorobenzylidene derivatives > *o*-fluorobenzylidene derivatives > *p*-fluorobenzylidene derivatives. The biological activity of above sequence also occurred with bromine substituted benzylidene derivatives.

Conclusion

In summary, a series of Schiff bases bearing 1,2,4-triazole ring systems were synthesized. These were characterized by IR, ^1H NMR and elemental analyses. All the compounds were screened for their antifungal activity by mycelium growth rate method. The antifungal tests indicated that compounds **5t** and **5v** possessed excellent antifungal activities and could be further developed as fungicides.

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