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Synthesis and antifungal potential of 1,2,3-triazole and 1,2,4-triazole thiol substituted strobilurin derivatives

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β-Methoxyacrylate group is an important pharmacophore of commercially used strobilurin fungicides. In the present study, a total of seventeen 1,2,4-triazole thiols **8a-h** and 1,2,3-triazole substituted **10a-i** strobilurin derivatives have been synthesized. 1,2,4-Triazole thiol substituted strobilurin derivatives **8a-h** have been found to inhibit the growth of plant pathogens such as *Fusarium oxysporum*, *Magnaporthe grisea, Drechslera oryzae* and human pathogens *Aspergillus fumigatus* and different strains of *Cryptococcus neoformans*, with MIC in the range of 16-256 μg/mL. In case of *Candida albicans* tested strain, the MIC is > 256 μg/mL. *p*-Chlorophenyl substituted 1,2,4-triazole thiol strobiulrin derivative **8e** is the most potent inhibitor with MIC of 16-64 μg/mL against most of the tested pathogens. Antifungal action of the compounds is due to inhibition of mitochondrial respiration. In the resazurin reduction assay, EC_{50} for inhibition of RZ reduction in *D. oryzae* by azoxystrobin and **8e** are 3.42±0.03 μg/mL and 3.63±0.21 μg/mL, respectively; while in case of *C. neoformans,* EC_{50} of azoxystrobin and **8e** are between 0.65-0.85 μg/mL. In a non-pathogenic model *Benjaminiella poitrasii,* though the MIC for all the synthesized compounds **8a-h** and **10a-i** are > 256 μg/ml, yeast to hypha transition is inhibited in the range of 21-75% at 4 μg/mL concentration while EC_{50} for inhibition of RZ reduction by azoxystrobin and **8e** are 31.5 ±0.4 μg/mL and 17.95 ± 0.7 μg/mL, respectively. The 50% germ tube formation inhibition in case of *C. albicans* is observed at 108.49 μg/mL. 1,2,4-Triazole thiol substituted strobilurin derivatives hold promise for the control of pathogenic fungi in agriculture and health care.

Keywords: Strobilurin, 1,2,3-triazole strobilurin, 1,2,4-triazole thiol strobilurin, antifungal, Y-H transition inhibition

Strobilurins is a major class of fungicides used in agriculture[1]. Two antibiotics strobilurins A and B from the mycelium of *Strobilurus tenacellus* strain No. 21602 were isolated by Anke *et al.*[2] Thereafter, a number of different strobilurins such as strobilurin H, 9-methoxy-strobilurins L and K, strobilurin D and hydroxyl-strobilurin D were isolated from *Favolaschia calocera,* and strobilurin E was isolated from *Agaricus* (*Crepidotus*) *fulvotomentosus*[3-6]. These compounds were found to inhibit yeast such as *Candida albicans, Rhodotorula glutinis* and filamentous fungi including phytopathogens *Botrytis cinerea*, *Rhizoctonia solani, Cladosporium cladosporioides, Curvularia lunata, Phytophthora infestans* (now not classified as fungus), and others. General structure of strobilurin consists mainly of three parts-side chain, aromatic bridge and pharmacophore (*E*)-methyl-β-methoxyacrylate group or (*E*)-methylmethoxyiminoacetate group (**Figure 1**). Fungicidal action of strobilurins is due to their binding to the Q_o site of cytochrome b resulting in inhibition of mitochondrial respiration[7]. In 1996, first synthetic strobilurin, azoxystrobin came to agriculture scenario for the control of plant pathogenic fungi[1,8]. Many strobilurin derivatives were synthesized for use in agriculture fields. However plant pathogenic fungi developed resistance to these synthetic strobilurins[9,10].

1,2,3-Triazole is a potential pharmacophore due to its moderate dipole character and rigidity. Hence it can be readily incorporated into a molecule design strategy[11,12]. Secondly, a number of antifungal agents such as fluconazole, voriconazole, posaconazole, *etc*. consist of 1,2,4-triazole as a main pharmacophore[13-15]. In the present study, heterocycles 1,2,3-triazole or

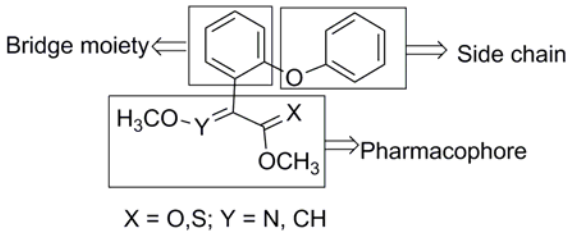


Figure 1 — General structure of strobilurin

1,2,4-triazole thiol moiety were incorporated in the general structure of strobilurin and were evaluated for their antifungal potential.

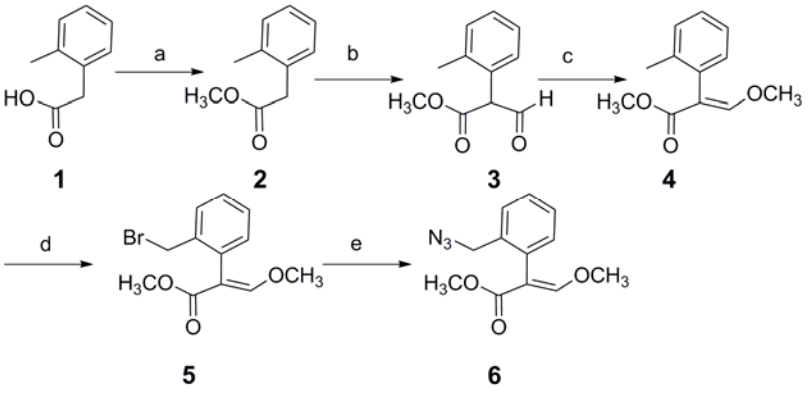
Results and Discussion

Synthesis

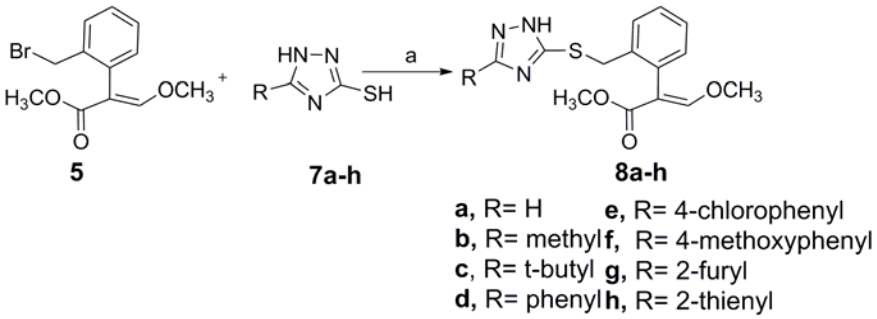
Synthesis of 1,2,4-triazole thiol substituted strobilurin derivatives, 8a-h. Synthesis of (*E*)-methyl-2-(2-(bromomethyl)phenyl)-3-methoxyacrylate **5** was carried out using reported procedure[16]. Synthesis was started with esterification of *o*-tolylacetic acid **1** to get corresponding ester **2**, which on further formylation gave **3**. Compound **3** was then reacted with dimethyl sulphate in presence of tetrabutyl ammonium bromide (TBAB) to get (*E*)-methyl-2-(methyl phenyl)-3-methoxyacrylate **4**. The yield of (*E*)-methyl-2-(methyl phenyl)-3-methoxyacrylate **4** was improved (98%) using phase transfer catalyst TBAB and specifically *E* isomer of **4** was obtained. Bromination of **4** was carried out using *N*-bromosuccinamide in carbon tetrachloride and AIBN as an initiator to get compound **5** (**Scheme I**).

Synthesis of 5-substituted-1,2,4-triazole-3-thiols **7a-h** was carried out according to the reported procedure[17]. Compound **5** was finally coupled with different 5-substituted-1,2,4-triazole-3-thiols **7a-h** in presence of K_2CO_3 to get compounds **8a-h** (**Scheme II**). Compounds **8a-h** were fully characterized using IR, ^1H and ^{13}C NMR, and mass spectrometry. For instance, ^1H NMR spectrum of compound **8a** showed resonance at δ 7.95 and 7.61 as singlet for 5C-H protons of triazole thiol and vinylic proton, along with two singlets at δ 3.85 and 3.77 for-OCH_3 protons. For S-CH_2 protons singlet was seen at δ 4.13.

Synthesis of 1,2,3-triazole substituted strobilurin derivatives, 10a-i. Compound **5** was transformed into (*E*)-methyl 2-(2-(azidomethyl)phenyl)-3-methoxy-acrylate **6** by S_N2 displacement of bromo group in presence of NaN_3 with 92% yield (**Scheme I**)[18]. Propargylated ethers of phenols **9a-i** were obtained by reacting phenols with propargyl bromide in presence



Scheme I — Reagents and conditions: (a) MeOH, drop of H_2SO_4, 28°C, 12 h, 98%; (b) Methyl formate, NaH, Toluene, 0-28°C,12 h, 98%; (c) Dimethyl sulphate, EDC/H_2O (1:1), TBAB, Na_2CO_3, 28°C, 2 h, 98%; (d) AIBN, NBS, CCl_4, 80°C, 3 h, 95%; (e) NaN_3, acetone, 60°C, 6 h, 92%



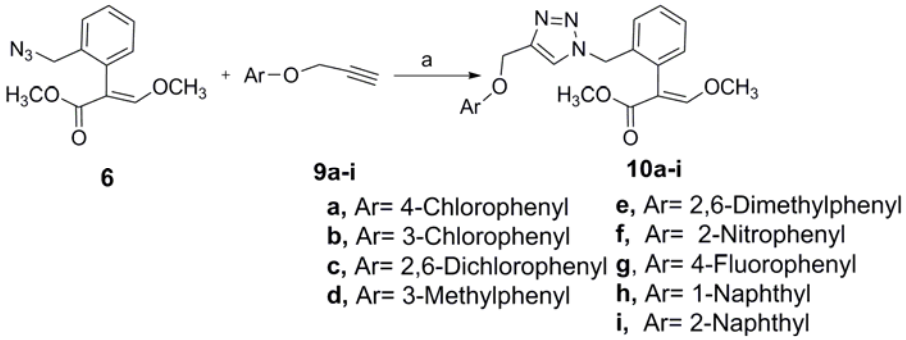
Scheme II — Reagents and conditions: (a) K_2CO_3, DMF, 28°C, 4-6 h

of K_2CO_3 in DMF[19]. 1,3-Dipolar cycloaddition of azide **6** and different propargylated phenols **9a-i** was carried out by Sharpless click reaction[20]. One equivalent of propargylated ether of phenols **9a-i** and one equivalent of azide **6** were dissolved in *t*-butanol/ water (10 mL) and the resulting solution was treated with 5 mol% $CuSO_4.5H_2O$ and 10 mol% sodium ascorbate to get compounds **10a-i** (**Scheme III**)[17]. All 1,2,3-triazolyl strobilurins were characterized by IR, ^1H and ^{13}C NMR, and mass spectrometry. For compound **10a,** ^1H NMR spectrum showed resonance at δ 7.57 as a singlet for triazole proton. A singlet at δ 7.44 for vinylic proton, two singlets at δ 5.43 and 5.11 for O-CH_2 and N-CH_2 protons and two singlets at δ 3.76, 3.67 for O-CH_3 protons were observed.

Biological activities

Antifungal activity of strobilurin derivatives

The 1,2,4-triazole thiol substituted strobilurin derivatives **8a-h** showed selective antifungal activity against the tested strains of plant and human fungal pathogens (**Table I**). From the series, *p*-chloro phenyl substituted derivative **8e** was the most potent inhibitor with MIC of 16-64 μg/mL against all the tested pathogens. Moreover, **8e** exhibited better activity in comparision to azoxystrobin against *Cryptococcus neoformans* NCIM 3378 and *C. neoformans* NCIM 3542. *C. neoformans* strain NCIM 3541 and *Drechslera oryzae* were found to be sensitive towards all 1,2,4-triazole thiol substituted strobilurin derivatives except **8h**. MIC values for both *C. albicans* and *Benjaminiella poitrasii* were > 256 μg/mL. There are few reports on azole substituted strobilurin derivatives. Chen *et al.* reported the synthesis of a library of antifungal triazoles modified β-methoxyacrylate analogues which were tested against *Alternaria brassicae, A. brassicola, Aspergillus flavus, F. oxysporum* and others. But none of the compounds showed MIC below 500 μg/mL[18]. Li and co-workers reported the synthesis of fifteen novel 5-aryl-2-mercapto-1,3,4-oxadiazoles substituted (*E*)-α-(methoxyimino)-benzeneacetate derivatives which showed antifungal activity against *Rhizoctonia solani, Botrytis cinerea, Gibberella zeae, Physalospora piricola* and *Bipolaris maydis*[21]. All these compounds inhibited 80-100% growth of all tested fungi at



Scheme III — Reagents and conditions: (a) $CuSO_4$, sodium ascorbate, *t*-BuOH/H_2O (8:2), 28°C, 3-6 h

Table I — Antifungal activities and difference in R groups for 1,2,4-triazole thiol substituted strobilurin derivatives

Inhibitor	R group	Minimum Inhibitory Concentration (MIC) in μg/mL						
		Plant pathogens			Human pathogens			
		Fusarium oxysporum	*Magnaporthe grisea*	*Drechslera oryzae*	*Cryptococcus neoformans* NCIM 3378	*C. neoformans* NCIM 3541	*C. neoformans* NCIM 3542	*Aspergillus fumigatus*
8a	H	>256	>256	256	>256	64	>256	>256
8b	Methyl	>256	128	128	>256	256	>256	>256
8c	t-Butyl	>256	>256	32	>256	64	>256	>256
8d	Phenyl	64	>256	64	256	64	128	128
8e	4-Chlorophenyl	64	16	16	16	64	64	64
8f	4-Methoxyphenyl	>256	32	64	>256	64	256	32
8g	2-furyl	256	64	128	>256	256	>256	256
8h	2-thienyl	>256	128	256	>256	>256	>256	>256
Azoxystrobin		32	4	16	32	16	128	4

50 µg/mL concentration. Shridhara *et al.* synthesized different 3-isoxazoline methyl-3-methoxy-2-(4-oxo-3,4-dihydrophthalazin-1-yl)prop-2-enoate derivatives and among them compounds with 4-chlorophenyl and 4-fluorophenyl substituent showed potent inhibition of *Aspergillus niger* and *C. albicans* with MIC 62.5 µg/mL[22]. For pyrazole β-methoxyacrylate analogues, compounds with *p*-chlorophenyl substituent were more effective against *Pseudoperonospora cubensis* and *Erysiphe graminis* in comparision to *Pyricularia oryzae* and *B. cinerea*[23]. Zhao *et al.* also showed that in case of chalcone based derivatives, 4-chlorophenyl substituted derivative showed >99% growth inhibition of *P. cubensis*, and *Sphaerotheca fuliginea* at 200 µg/mL concentration[24]. Similarly, in the present study compound **8e** with 4-chlorophenyl substituent showed good antifungal activity against different pathogenic fungi. The 1,2,3-triazole substituted strobilurin derivatives **10a-i** were ineffective in controlling the growth of the fungal pathogens at the highest concentration (512 µg/mL) tested. The results indicated that 1,2,4-triazole thiol group played an important role in the antifungal activity exhibited by **8a-h**.

Inhibition of resazurin reduction

The oxidized form of resazurin (RZ) is non-fluorescent and blue in color. Inside a microbial cell in response to the cellular metabolism, it is reduced to a fluorescent and pink colored resorufin and the change can be monitored fluorometrically or spectrophotometrically[25,26]. The percent RZ reduction corresponds to the fungal respiration rate as this RZ reduction takes place in the cytochrome oxidase region, during the final reduction of O_2 and the cytochrome a-a_3 complex. The observed EC_{50} for inhibition of RZ reduction in *D. oryzae* by azoxystrobin and **8e** were 3.42±0.03 µg/mL and 3.63±0.21 µg/mL, respectively (**Figure 2**). In case of the yeast *C. neoformans* NCIM 3378, both azoxystrobin and **8e** were effective at EC_{50} 0.69 ± 0.1 µg/mL and 0.82 ± 0.05 µg/mL, respectively. For *C. albicans*, EC_{50} values were 56.2 ± 1.2 µg/mL and 35.8 ± 2.1 µg/mL for **8e** and azoxystrobin, respectively. Whereas EC_{50} values of 17.95 ± 0.7 µg/mL and 31.5 ± 0.4 µg/mL for **8e** and azoxystrobin, respectively were observed for *B. poitrasii*. The inhibition of RZ reduction by compounds **8e** indicated that these compounds exhibit similar mode of action as azoxystrobin *i.e.* they inhibit mitochondrial respiration by binding to the Q_o site of cytochrome b.

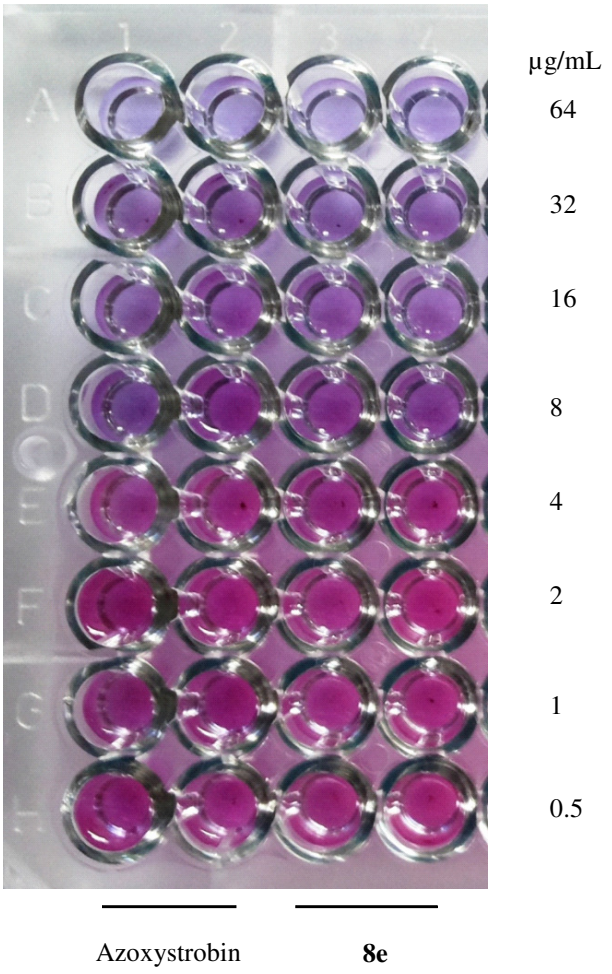


Figure 2 — Inhibition of resazurin reduction in *Drechslera oryzae* by compounds (a) azoxystrobin, and (b) **8e**

Inhibition of yeast to hypha transition

Most of the pathogenic fungi exhibit two morphological forms namely yeast and hyphal form for survival in the host. Transition from one form to another is required for pathogenesis and compounds which retard this dimorphic transition may have potential as antifungal drugs[27]. Hawser *et al.* tested eleven antifungal agents for their morphogenetic transition inhibition and growth inhibition in *C. albicans*[28]. It was observed that antifungal agents amphotericin B, mulundocandin and aculeacin inhibited morphogenetic transformation at concentrations lower than their MIC. This proves that inhibition of germ tube formation is more sensitive towards antifungal agent action than inhibition of growth. All 1,2,3-triazole and 1,2,4-triazole thiol substituted strobilurin derivatives were tested for their potential to inhibit Y-H transition inhibition (germ tube formation inhibition) of *B. poitrasii*

Table II — Inhibition of germ tube formation in *Benjaminiella poitrasii* by 1,2,4-triazole thiol and 1,2,3-triazole substituted strobilurin derivatives

Inhibitor (4 μg/mL)	Inhibition of germ tube formation (%)	Inhibitor (4 μg/mL)	Inhibition of germ tube formation (%)
8a	47.24	**10a**	30.00
8b	41.71	**10b**	24.90
8c	75.50	**10c**	21.36
8d	45.50	**10d**	40.05
8e	66.13	**10e**	55.89
8f	44.18	**10f**	34.93
8g	41.93	**10g**	32.60
8h	47.61	**10h**	43.69
Azoxystrobin	77.00	**10i**	44.79

at 4 μg/mL concentration. *B. poitrasii* has been established as a model to study fungal differentiation and to screen antifungal compounds which affect the differentiation[19,29]. 1,2,4-Triazole thiol substituted strobilurin derivatives **8a-h** inhibited Y to H transition in the range 41-75%. Compound **8c** with *t*-butyl substituent was found to be the most potent inhibitor of transition (75.5%). Compound **8e** with *p*-chlorophenyl substituent showed 66% inhibition of Y-H transition. 1,2,3-Triazole substituted strobilurin derivatives **10a-i** showed 21-56% inhibition of Y-H transition (**Table II**). Compound **10d** and **10e** with methyl substituent showed 40 and 55% of Y-H transition inhibition respectively. Napthyl substituted 1,2,3-triazole substituted strobilurin derivatives **10h** and **10i** showed 44% of transition inhibition. Compounds **10a-c**, **10f** and **10g** with electron withdrawing substituent showed lower transition inhibition (21-34%). Whereas, in case of *C. albicans*, 108.49 ±0.21 μg/mL concentration of **8e** was required for 50% inhibition of germ tube formation.

Hemolysis

The concentration causing 50% hemolysis (HC_{50}) for all 1,2,4-triazole thiol and 1,2,3-triazolyl β-methoxyacrylate compounds was >1000 μg/mL. As hemolysis was not observed at the MIC values of all these compounds, they may be explored further for their potential as antifungal agents.

Experimental Section

Synthesis of methyl 2-tolylacetate, 2. *o*-Tolylacetic acid **1** (1 g, 6.6 mmol) was dissolved in methanol. Catalytic amount of sulfuric acid was (0.2 mL) added to this solution. The mixture was stirred at RT for 12 h. Reaction completion was checked by TLC. Excess methanol was evaporated and 25 mL water was added. Product was extracted into 2×150 mL ethyl acetate. Ethyl acetate layer was washed sequentially with 2×25 mL $NaHCO_3$ solution, 25 mL water and 25 mL brine solution. The organic layer was dried over anhyd. Na_2SO_4 and concentrated under reduced pressure to yield 1.09 g (98%) of methyl 2-tolylacetate **2** in the form of colorless oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.29 (m, 4H), 3.81 (s, 2H), 3.63 (s, 3H), 2.28 (s, 3H); ^{13}C ($CDCl_3$, 50MHz): δ 171.92, 162.98, 131.13, 130.12, 129.84, 128.02, 127.58, 125.71, 51.67, 38.79, 19.87; MS: *m/z* 187 $[M+Na]^+$; IR ($CHCl_3$): 1724, 1369, 1174, 1024 cm^{-1}. Anal. Calcd for $C_{11}H_{12}O_3$: C, 73.15; H, 7.37. Found: C, 73.10; H, 7.37%.

Synthesis of methyl-3-oxo-2-*o*-tolylpropanoate, 3. To a solution of methyl 2-tolylacetate **2** (1 g, 6.09 mmol) in toluene (5 mL), methyl formate (5.6 mL) was added. Sodium hydride (0.29 g, 12 mmol) was added to this mixture in small portions over a period of 1 h at 0°C under argon atmosphere. Reaction mixture was stirred at 28°C for 12 h. After completion of reaction (monitored by doing TLC), excess methyl formate and toluene were evaporated under reduced pressure and the reaction mixture was quenched with ice. Product was extracted with 150 mL of ethyl acetate. Organic layer was washed sequentially with 2×50 mL of water and 50 mL of brine solution and dried over anhyd. Na_2SO_4. The solvent was then evaporated under reduced pressure to get a brown colored oil which on further purification by column chromatography using ethyl acetate-petroleum ether afforded 1.05 g (98%) of methyl-3-oxo-2-*o*-tolylpropanoate **3**. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 11.93 (d, 1H), 7.29 (m, 4H), 3.81 (s, 3H), 3.73 (s, 1H), 2.28 (s, 3H); ^{13}C ($CDCl_3$, 50MHz): δ 171. 92, 162.98, 131.13, 130.12, 129.84, 128.02, 127.58, 125.71, 51.67, 38.79, 19.87; MS: *m/z* 215 $[M+Na]^+$; IR ($CHCl_3$): 2981, 1724, 1658, 1369, 1174, 1024, 827 cm^{-1}. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.78; H, 6.24. Found: C, 68.82; H, 6.00%.

Synthesis of (*E*)-methyl-2-(methylphenyl)-3-methoxy-acrylate, 4. The methyl 3-oxo-2-*o*-tolyl-propanoate **3** (1 g, 5.2 mmol) was taken in 10 mL ethylene dichloride/water (1:1). To this heterogeneous solution sodium carbonate (0.66 g, 6.24 mmol) and catalytic amount of tetrabutyl-ammonium bromide (TBAB) was added, followed by addition of dimethyl sulfate (0.787 g, 6.25 mmol). This heterogenous

mixture was stirred at RT for 2 h. Completion of reaction was checked by TLC. Organic layer was separated from water layer and sequentially washed with 2×25 mL of water, 25 mL brine and dried over anhyd. Na_2SO_4. The solvent was evaporated to get final product (*E*)-methyl 2-(methyl phenyl)-3-methoxy-acrylate **4** (1.05 g, 98%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.56 (s, 1H), 7.18 (m, 4H), 3.80 (s, 3H), 3.69 (s, 3H), 2.18 (s, 3H); ^{13}C ($CDCl_3$, 50MHz): δ 164.5, 158.3, 136.1, 134.6, 131.3, 127.8, 126.3, 125.26, 104.0, 60.2, 52.3, 19.2; MS: *m/z* 229.24 $[M+Na]^+$; IR ($CHCl_3$): 2948, 1708, 1631, 1255, 1130 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.92; H, 6.79%.

Synthesis of (*E*)-methyl-2-(2-(bromomethyl)phenyl)-3-methoxyacrylate, 5. To a solution of (*E*)-methyl-2-(methylphenyl)-3-methoxyacrylate **4** (1 g, 4.8 mmol) in carbon tetrachloride (10 mL) azaisobutyronitrile (AIBN, 0.078 g, 0.48 mmol) and N-bromosuccinamide (1.02 g, 5.76 mmol) was added. The reaction mixture was refluxed for 3 h. After completion of reaction (checked by TLC), carbon tetrachloride was removed under reduced pressure and the residue was extracted into ethyl acetate. Ethyl acetate layer was sequentially washed with 2 x 25 mL of water, 25 mL brine and dried over anhyd. Na_2SO_4. The solvent was then evaporated to get crude product, which on purification by column chromatography using ethyl acetate and petroleum ether as eluent afforded 1.31 g (95%) of (*E*)-methyl 2-(2-(bromomethyl)-phenyl)-3-methoxy-acrylate **5**. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.63 (s, 1H), 7.44 (m, 2H), 7.33 (m, 2H), 4.40 (s, 2H) 3.82 (s, 3H), 3.69 (s, 3H); ^{13}C ($CDCl_3$, 50MHz): δ 164.5, 158.3, 136.1, 134.6, 131.3, 127.8, 126.3, 125.26, 101.0, 60.2, 52.3, 51.56; MS: *m/z* 307 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631, 1434, 765 cm^{-1}. Anal. Calcd for $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60. Found: C, 50.70; H, 4.50%.

Synthesis of (*E*)-methyl-2-(2-(azidomethyl)phenyl)-3-methoxyacrylate, 6. To a solution of (*E*)-methyl 2-(2-(bromomethyl)-phenyl)-3-methoxyacrylate **5** (1g, 3.05 mmol) in 15 mL of acetone, sodium azide (0.237 g, 3.66 mmol) was added. The reaction mixture was stirred at 60°C for 6 h. On completion of the reaction (monitored by TLC), acetone was removed under vacuum and extracted with 256 mL of ethyl acetate. Ethyl acetate layer was washed sequentially with 4×25 mL of water and 25 mL of brine solution. Organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield crude product. The purification of crude product by silica gel column chromatography using ethyl acetate-petroleum ether mixture as eluent gave 0.8 g (92.3%) of (*E*)-methyl 2-(2-(azidomethyl)phenyl)-3-methoxyacrylate **6**. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.60 (s, 1H), 7.40 (m, 4H), 3.90 (s, 2H), 3.72 (s, 3H), 3.69 (s, 3H); ^{13}C ($CDCl_3$, 50MHz): δ 64.5, 158.3, 136.1, 134.6, 131.3, 128.8, 126.3, 125.62, 111.0, 60.2, 52.3, 49.00; MS: *m/z* (MH^+) 283; IR ($CHCl_3$): 2110, 1708, 1631, 1434, 765 cm^{-1}. Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 16.99. Found: C, 58.70; H, 5.45; N,16.40%.

General procedure for the synthesis of 1,2,4-triazole thiol substituted strobilurin derivatives, 8a-h

5-Substituted-1,2,4-triazole-3-thiols **7a-h** (1 mmol) was dissolved in DMF (10 mL) to which K_2CO_3 (1.2 mmol) was added, followed by the dropwise addition of solution of (*E*)-methyl 2-(2-(bromomethyl)phenyl)-3-methoxyacrylate **5** in DMF (5 mL). Reaction mixture was stirred at RT for a period of 4 h. After completion of reaction (checked by TLC), the reaction mixture was quenched with ice and extracted with ethyl acetate. The ethyl acetate layer was washed subsequently with 3×35 mL of water, 35 mL of brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. Finally the crude product obtained was purified by silica gel column chromatography using ethyl acetate and petroleum ether as eluent to afford **8a-h**.

(*E*)-Methyl-2-(2-((1*H*-1,2,4-triazol-3-ylthio)methyl)-phenyl)-3-methoxyacrylate, 8a: Yield 70%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (s, 1H), 7.61 (s, 1H), 7.15 (m, 4H), 4.13 (s, 2H), 3.85 (s, 3H), 3.77 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 160.30, 150.01, 135.58, 132.18, 131.52, 129.43, 128.44, 127.89, 110.27, 62.16, 51.08, 36.02; MS: *m/z* 328.08 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{14}H_{15}N_3O_3S$: C, 55.07; H, 4.95; N, 13.76, S, 10,50. Found: C, 55.20; H, 5.0, N, 13.89; S, 11.02%.

(*E*)-Methyl-3-methoxy-2-(2-((5-methyl-1*H*-1,2,4-triazol-3-ylthio)methyl)phenyl) acrylate, 8b: Yield 70%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62 (s, 1H), 7.21 (m, 4H), 4.18 (s, 2H), 3.86 (s, 3H), 3.76 (s, 3H), 2.43 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 168.58, 160.75, 155.62, 135.68, 132.43, 131.39, 129.70, 128.30, 127.72, 109.82, 62.18, 51.93, 35.30, 12.03; MS: *m/z* 342.38 $[M+Na]^+$; IR ($CHCl_3$): 3419, 1710, 1660 cm^{-1}. Anal. Calcd for $C_{15}H_{17}N_3O_3S$: C, 56.41; H, 5.37; N, 13.16. Found: C, 56.30; H, 5.50, N, 12.90%.

(*E*)-Methyl-3-methoxy-2-(2-((5-*t*-butyl-1*H*-1,2,4-triazol-3-ylthio)methyl)phenyl) acrylate, 8c: Yield 75%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60 (s, 1H), 7.16 (m, 4H), 4.12 (s, 2H), 3.85 (s, 3H), 3.76 (s, 3H), 1.34 (s,

9H); ^{13}C ($CDCl_3$, 400MHz): δ 160.20, 135.93, 132.24, 131.41, 129.65, 128.83, 128.26, 127.73, 110.38, 71.81, 62.09, 51.98, 35.89, 32.47, 29.14, 19.15; MS: *m/z* 384.15 $[M+Na]^+$; IR ($CHCl_3$): 1719, 1632 cm^{-1}. Anal. Calcd for $C_{18}H_{23}N_3O_3S$: C, 59.81; H, 6.41; N, 11.63. Found: C, 59.99; H, 6.55, N, 11.70%.

(*E*)-Methyl-3-methoxy-2-(2-((5-phenyl-1*H*-1,2,4-triazole-3-ylthio)methyl)phenyl) acrylate, 8d: Yield 75%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07 (m, 2H), 7.61 (s, 1H), 7.40 (m, 4H), 7.15 (m, 3H), 4.21 (s, 2H), 3.83 (s, 3H), 3.75 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 69.74, 162.25, 137.54, 134.10, 132.65, 131.34, 130.73, 130.00, 129.62, 129.29, 128.94, 128.65, 128.44, 127.38, 111.01, 62.44, 52.07, 36.25; MS: *m/z* 404.11 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1633 cm^{-1}. Anal. Calcd for $C_{20}H_{19}N_3O_3S$: C, 62.97; H, 5.02; N, 11.02. Found: C, 62.95; H, 4.98; N, 11.56%.

(*E*)-Methyl-3-methoxy-2-(2-((5-(4-clorophenyl)-1*H*-1,2,4-triazole-3-ylthio)methyl) phenyl) acrylate, 8e: Yield 82%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98 (d, 2H, *J* = 12Hz), 7.63 (s, 1H), 7.38 (d, 2H, *J* = 8 Hz), 7.15 (m, 4H), 4.13 (s, 2H), 3.87 (s, 3H), 3.80 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 68.86, 160.59, 135.80, 135.40, 132.18, 131.47, 129.53, 128.85, 128.42, 127.81, 127.67, 110.05, 62.11, 52.03, 35.89; MS: *m/z* 438.89 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1633 cm^{-1}. Anal. Calcd for $C_{20}H_{18}ClN_3O_3S$: C, 57.76; H, 4.36; Cl, 8.52; N, 10.10. Found: C, 57.86; H, 4.20; Cl, 9.52; N, 10.40%.

(*E*)-Methyl-3-methoxy-2-(2-((5-(4-methoxyphenyl)-1*H*-1,2,4-triazole-3-ylthio) methyl)phenyl) acrylate, 8f: Yield 71%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, 2H, *J* = 8 Hz), 7.61 (s, 1H), 7.18 (m, 4H), 6.93 (d, 2H, *J* = 12 Hz), 4.16 (s, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.77 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 168.69, 160.74, 160.44, 136.03, 132.17, 131.32, 129.60, 128.32, 127.83, 127.61, 114.01, 110.10, 62.03, 55.25, 51.92, 35.68; MS: *m/z* 434.47 $[M+Na]^+$; IR ($CHCl_3$): 708, 1631 cm^{-1}. Anal. Calcd for $C_{21}H_{21}N_3O_4S$: C, 61.30; H, 5.14; N, 10.21. Found: C, 61.39; H, 5.50; N, 9.98%.

(*E*)-Methyl-3-methoxy-2-(2-((5-(furan-2-yl)-1*H*-1,2,4-triazol-3-ylthio)methyl) phenyl) acrylate, 8g: Yield 73%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (s, 1H), 7.51 (d, 1H, *J* = 4Hz), 7.21 (m, 4H), 6.99 (d, 1H, *J* = 4Hz), 6.51 (dd, 1H, *J* = 4Hz), 4.17 (s, 2H), 3.88 (s, 3H), 3.80 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 168.66, 160.48, 144.78, 143.42, 135.55, 132.20, 131.35, 129.51, 128.34, 127.72, 111.51, 109.96, 62.03, 51.91, 35.61; MS: *m/z* 394.09 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{18}H_{17}N_3O_4S$: C, 58.21; H, 4.61; N, 11.31. Found: C, 58.90; H, 4.85; N, 11.65%.

(*E*)-Methyl-3-methoxy-2-(2-((5-(thiophen-2-yl)-1*H*-1,2,4-triazol-3-ylthio)methyl) phenyl) acrylate, 8h: Yield 52%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (d, 1H, *J* = 4Hz), 7.62 (s, 1H), 7.32 (d, 1H, *J* = 4Hz), 7.16 (m, 4H), 7.07 (dd, 1H, *J* = 4Hz), 4.12 (s, 2H), 3.86 (s, 3H), 3.79 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 168.92, 160.45, 135.59, 132.15, 131.54, 129.51, 128.54, 127.95, 127.70, 126.68, 126.39, 110.22, 62.17, 51.11, 36.08; MS: *m/z* 410.07 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{18}H_{17}N_3O_3S_2$: C, 55.80; H, 4.42; N, 10.84. Found: C, 56.01; H, 4.10; N, 10.98%.

General procedure for the synthesis of 1,2,3-triazole substituted strobilurin derivatives, 10a-i

To a stirred solution of (*E*)-methyl 2-(2-(azidomethyl)-phenyl)-3-methoxyacrylate **6** (1 mmol) and specific propargyl ethers of phenols **9a-i** (1 mmol) in 10 mL of tertiary butanol/water (8:2), copper sulphate (24 mg, 5 mol %) and sodium ascorbate (40 mg, 10 mol %) were added. Reaction mixture was stirred at 28°C for 3-6 h. On completion of the reaction (monitored by TLC), *t*-butanol was removed under reduced pressure and the reaction mixture was partitioned between ethyl acetate and water. The ethyl acetate layer was washed subsequently with 3×35 mL of water, 35 mL of brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get crude product. Finally, the crude product was purified by silica gel column chromatography using ethyl acetate and petroleum ether as eluent to obtain pure 1,2,3-triazole derivatives of strobilurin **10a-i**.

(*E*)-Methyl-2-(2-((4-((4-chlorophenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10a: Yield 68%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61 (s, 1H), 7.44 (s, 1H), 7.35 (m, 2H), 7.20 (m, 4H), 7.09 (d, 1H, *J* = 8Hz), 6.88 (d, 1H, *J* = 8Hz), 5.43 (s, 2H), 5.11 (s, 2H), 3.76 (s, 3H), 3.67 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.10, 160.77, 156.82, 133.49, 131.75, 129.39, 129.04, 128.78, 128.68, 116.07, 109.38, 62.27, 62.11, 52.23, 51.80; MS: *m/z* 436.11 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal Calcd for $C_{21}H_{20}ClN_3O_4$: C, 60.95; H, 4.87; N, 10.15. Found: C, 60.40; H, 5.01; N,10.94%.

(*E*)-Methyl-2-(2-((4-((2-chlorophenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10b: Yield 60%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62 (s, 1H), 7.50 (s, 1H), 7.35 (m, 3H), 7.20 (t, 3H, *J* = 8Hz), 7.09 (d, 1H, *J* = 8Hz), 6.90 (t, 1H, *J* = 8Hz), 5.43 (s, 2H), 5.23 (s, 2H), 3.76 (s, 3H), 3.67 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.43, 160.85, 153.73, 143.68, 133.49, 132.46, 131.69, 130.28, 130.28, 128.97, 128.68, 128.60,

127.80, 123.16, 122.91, 121.97, 114.22, 109.28, 63.14, 62.11, 52.16, 51.76; MS: *m/z* 436.11 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{21}H_{20}ClN_3O_4$: C, 60.95; H, 4.87; N, 10.15. Found: C, 60.40; H, 5.01; N,10.10%.

(*E*)-Methyl-2-(2-((4-((2,6-dichlorophenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10c: Yield 56%; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.61 (s, 1H), 7.49 (s, 1H), 7.37 (m, 2H), 7.21 (m, 1H), 7.00 (m, 4H), 5.56 (s, 2H), 4.90 (s, 2H), 3.79 (s, 3H), 3.68 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.12, 160.44, 155.00, 144.54, 134.31, 132.04, 130.74, 130.69, 128.61, 128.50, 128.32, 123.85, 122.47, 109.03, 65.23, 61.80, 51.78, 51.45; MS: *m/z* 470.08 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{21}H_{19}Cl_2N_3O_4$: C, 56.26; H, 4.27; N, 9.37. Found: C, 56.62; H, 4.52; N, 9.32%.

(*E*)-Methyl-2-(2-((4-((3-methylphenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10d: Yield 70%; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.61 (s, 1H), 7.43 (s, 1H), 7.36 (m, 2H), 7.12 (m, 3H), 6.76 (t, 3H, *J* = 8Hz), 5.43 (s, 2H), 5.13 (s, 2H), 3.75 (s, 3H), 3.67 (s, 3H), 2.31 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.23, 160.64, 158.08, 144.05, 139.35, 133.41, 132.32, 131.53, 129.03, 128.85, 128.50, 128.42, 122.71, 121.81, 115.33, 111.39, 109.12, 61.89, 61.73, 51.98, 51.55, 21.31; MS: *m/z* 416.17 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{22}H_{23}N_3O_4$: C, 67.16; H, 5.89; N, 10.68. Found: C, 67.96; H, 6.01; N, 10.94%.

(*E*)-Methyl-2-(2-((4-((2,6-dimethylphenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10e: Yield 55%; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.59 (s, 1H), 7.49 (s, 1H), 7.37 (m, 2H), 7.21 (m, 2H), 6.96 (m, 3H), 5.46 (s, 2H), 4.90 (s, 2H), 3.79 (s, 3H), 3.68 (s, 3H), 2.22 (s, 6H); ^{13}C ($CDCl_3$, 400MHz): δ 167.12, 160.44, 155.00, 144.31, 133.31, 132.04, 131.34, 130.69, 128.61, 128.50, 128.32, 123.85, 122.47, 109.03, 65.23, 61.80, 51.78, 51.45, 15.99; MS: *m/z* 430.18 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{23}H_{25}N_3O_4$: C, 67.80; H, 6.18; N, 10.31. Found: C, 67.50; H, 6.99; N,10.64%.

(*E*)-Methyl-2-(2-((4-((2-nitrophenoxy)methyl) - 1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10f: Yield 50%; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.81 (dd, 1H, *J* = 8Hz), 7.60 (s, 1H), 7.55 (s, 1H), 7.34 (m, 3H), 7.18 (d, 2H, *J* = 8Hz), 7.05 (t, 1H, *J* = 8Hz), 5.44 (s, 2H), 5.31 (s, 2H), 3.78 (s, 3H), 3.68 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.46, 160.88, 151.49, 140.08, 134.24, 133.46, 132.41, 131.69, 128.88, 128.71, 128.62, 125.58, 121.00, 115.42, 109.30, 63.64, 62.17, 52.20, 51.79; MS: *m/z* 447.14 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{21}H_{20}N_4O_6$: C, 59.43; H, 4.75; N, 13.20. Found: C, 59.94; H, 4.63; N, 13.62%.

(*E*)-Methyl-2-(2-((4-((4-fluorophenoxy)methyl) - 1*H*-1,2,3-triazol-1-yl)methyl) phenyl)-3-methoxyacrylate, 10g: Yield 65%; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.57 (s, 1H), 7.34 (m, 2H), 7.20 (d, 1H, *J* = 4Hz), 7.16 (d, 1H, *J* = 4Hz), 6.90 (m, 4H), 5.42 (s, 2H), 5.08 (s, 2H), 3.74 (s, 3H), 3.66 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.23, 160.66, 159.60, 154.86, 154.17, 154.12, 133.36, 132.31, 131.54, 128.80, 128.53, 128.43, 115.72, 109.09, 62.32, 61.91, 52.04, 51.56; MS: *m/z* 420.14 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{21}H_{20}FN_3O_4$: C, 63.47; H, 5.07; F, 4.78; N, 10.57. Found: C, 63.74; H, 5.60; F, 5.02; N,10.98%.

(*E*)-Methyl-3-methoxy-2 - (2-((4-((naphthalen-1-yloxy)methyl)-1*H*-1,2,3-triazol-1-yl) methyl) phenyl) acrylate, 10h: Yield 70%; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, 2H, *J* = 8Hz), 7.78 (d, 2H, *J* = 8Hz), 7.57 (s, 1H), 7.52 (s, 1H), 7.40 (m, 6H), 7.27 (t, 2H, *J* = 8Hz), 6.95 (d, 1H, *J* = 8Hz), 5.46 (s, 2H), 5.36 (s, 2H), 3.72 (s, 3H), 3.66 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.28, 160.64, 153.76, 134.29, 133.43, 132.25, 131.55, 128.76, 128.51, 128.47, 127.28, 126.25, 125.65, 125.37, 125.04, 122.81, 121.79, 120.59, 109.14, 105.19, 62.19, 61.89, 52.01, 51.59; MS: *m/z* 452.17 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{25}H_{23}N_3O_4$: C, 69.92; H, 5.40; N, 9.78. Found: C, 70.06; H, 5.94; N,10.06%.

(*E*)-Methyl-3-methoxy-2-(2 - ((4-((naphthalen-2-yloxy)methyl)-1*H*-1,2,3-triazol-1-yl) methyl) phenyl) acrylate, 10i: Yield 74%; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.76 (m, 3H), 7.59 (s, 1H), 7.51 (s, 1H), 7.38 (m, 4H), 7.21 (m, 4H), 5.47 (s, 2H), 5.30 (s, 2H), 3.77 (s, 3H), 3.69 (s, 3H); ^{13}C ($CDCl_3$, 400MHz): δ 167.05, 160.41, 155.75, 134.00, 133.14, 132.10, 131.33, 129.11, 128.67, 128.34, 128.26, 127.21, 126.50, 126.06, 123.47, 122.61, 118.36, 108.94, 106.74, 61.68, 51.84, 51.39, 37.77; MS: *m/z* 452.17 $[M+Na]^+$; IR ($CHCl_3$): 1708, 1631 cm^{-1}. Anal. Calcd for $C_{25}H_{23}N_3O_4$: C, 69.92; H, 5.40; N, 9.78. Found: C, 70.06; H, 5.94; N,10.06%.

Biological assays

Antifungal susceptibility testing

The synthesized compounds **8a-h** and **10a-i** were evaluated for their antifungal activity against human pathogens *C. albicans* NCIM 3557, three strains of *C. neoformans* (NCIM 3378, NCIM 3541, NCIM 3542), *Aspergillus fumigatus* NCIM 902 and plant pathogens, *Fusarium oxysporum* NCIM 1043, *Magnaporthe grisea, D. oryzae* and a non-pathogenic, dimorphic model fungus

B. poitrasii using standard broth micro-dilution technique as per Clinical Laboratory Standards Institute (CLSI) guidelines[30,31].

Resazurin based microtiter assay of Qo inhibitor sensitivity

A microtiter assay based on percent reduction of resazurin developed by Vega *et al*. was used to determine the fungicidal mode of action of the strobilurin derivatives in *D. oryzae, C. neoformans* NCIM 3378, *C. albicans* NCIM 3557 and *B. poitrasii*[32]. Briefly, appropriate stock solutions of compound **8e** and azoxystrobin were prepared by dissolving in dimethyl sulfoxide (DMSO), which was further serially diluted in the wells of a microtiter plate column. Using multichannel pipette, specific amount (4 µL), from these wells were added into other columns, so that final concentrations of the compound in wells of a column with 200 µL total volume will be 64, 32, 16, 8, 4, 2, 1, 0.5 µg/mL. To these wells, 20 µL of 400 µM resazurin and 176 µL YPG medium (0.3% yeast extract, 0.3% peptone, 0.4% glucose) containing 10^3 conidia (for *D. oryzae*) or yeast cells/mL. The plates were incubated in a rotary shaker-incubator (180 rpm) for 24 h at 28°C. After incubation, absorbance was measured at 570 and 600 nm. Percent RZ reduction was calculated based on the absorbance using formula:

$$\text{Percent resazurin reduction} = \frac{(\varepsilon_{OX})_{\lambda 2} A_{A1} - (\varepsilon_{OX})_{\lambda 1} A_{A2}}{(\varepsilon_{RED})_{\lambda 1} A'_{\lambda 2} - (\varepsilon_{RED})_{\lambda 2} A'_{\lambda 1}} \times 100$$

Where, ε_{OX} = molar extinction coefficient of RZ oxidized form (blue; 80,586 and 117,216 for 570 and 600 nm, respectively); ε_{RED} = molar extinction coefficient of RZ reduced form (pink; 155,677 and 14,652 for 570 and 600 nm, respectively); A = absorbance of test wells; A' = absorbance of negative control wells; λ1 = 570 nm; and λ2 = 600 nm.

The effective concentration needed to reduce RZ by 50% (EC_{50}) in micrograms per milliliter was calculated by using an exponential decay function:

$RZ(lc) = ae^{-blc}$

Where, $RZ(lc)$ = percent RZ reduction, lc = fungicide concentration, a = constant at initial lc value, and b = slope coefficient[32].

Inhibition of yeast to hypha transition

B. poitrasii, was used as a model to check the effect of synthesized compounds on yeast to hypha (% germ tube formation) transition[33]. Yeast inoculum was grown in YPG (Glucose 1%) medium at 37°C for 24 h and the transition to the hyphal form was studied in YP medium at 28°C. The yeast cells were inoculated in YP broth (with 4 µg/mL inhibitor and without inhibitor) and incubated at 28°C for 6 h. The percentage of cells forming germ tubes was assessed as described earlier[33]. For *C. albicans* NCIM 3557, yeast cells (1×10^6 cfu/mL) were inoculated in YPG broth supplemented with 10% fetal bovine serum (with different concentrations of inhibitor) and incubated at 37°C for 6 h. The percentage of cells forming germ tubes was assessed microscopically.

Hemolysis assay

All the compounds were tested for RBC hemolysis as described previously[34]. The concentrations tested were in the range of 4–1000 µg/mL.

Conclusion

In conclusion, total seventeen new strobilurin derivatives containing different 1,2,3-triazoles and 1,2,4-triazole thiols were synthesized using simple methods with good yields. 1,2,4-triazole thiol substituted strobilurin derivatives demonstrated good antifungal activity against human pathogens and phytopathogens. The compounds caused inhibition of mitochondrial respiration. All the compounds were found to be non-haemolytic. Further detailed investigations of the synthesized compounds and synthesis of newer similar compounds may yield a prospective candidate for the control of pathogenic fungi in agriculture and health care.

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