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Chiral γ-Aryl-1*H*-1,2,4-triazole Derivatives as Highly Potential Antifungal Agents: Design, Synthesis, Structure, and in Vitro Fungicidal Activities

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A novel series of chiral γ-aryl-1*H*-1,2,4-triazole derivatives as highly potential antifungal agents have been designed and synthesized conveniently by using the chiral auxiliary as a controlling reagent. All of the compounds exhibit moderate to high ee values reaching up to 99%, and the preliminary bioassay results demonstrated that most of the target compounds take on a significantly wide spectrum activity against *Fusarium oxysporium*, *Rhizoctonia solani*, *Botrytis cinereapers*, *Gibberella zeae*, *Dothiorella gregaria*, and *Colletotrichum gossypii* species.

KEYWORDS: Synthesis; chirality; 1,2,4-triazole; antifungal activities

INTRODUCTION

The application of agrochemicals to protect vegetable and cereal crops is an established part of conventional agriculture. This has provided healthy crops and increased yields as well as economic benefits for over many years. The main purpose of the research for agrochemicals is to develop novel active compounds with lower application doses, high selectivity, and reduced undesired environmental impact (*1, 2*). The azole fungicides, which were synthesized for the first time in the early 1970s for the protection of various crops, represent an important class of agrochemicals (*3*). The introduction of these sterol biosynthesis inhibitors represented a significant progress in the chemical control of fungal diseases. This class of pesticide includes several excellent systemic fungicides with long, protective, and curative activity against a broad spectrum of foliar, root, and seedling diseases caused by many ascomycetes, basidiomycetes, and imperfect fungi (*4, 5*).

Many of the most widely prescribed pesticides have optical isomers. At present, there are approximately 650 pesticides in the market, one-fourth of which have optical enantiomers. However, an important percentage is produced, marketed, and used in the form of racemates. The presence of a nonactive or less active stereoisomer only contributes to the increase of the levels of pollution without any benefit or relevant purpose. Therefore, the use of chiral pesticides has given rise to the research for new and effective methods of resolving enantiomeric mixtures. Triazole derivatives such as diniconazole, tebuconazole, hexaconazole, triadimefon, triadimenol, and so on (**Figure 1**) represent the most important category of fungicides to date. These compounds have excellent protective, curative, and eradicant power toward a wide spectrum of crop diseases, and they all have an asymmetrically substituted carbon atom leading to two enantiomers.

It is well-known that enantiomers can display different biological activities (*6*−*10*). Most of the published papers are focused on the separation of chiral pharmaceutical products as a result of the more severe guidelines for marketing new chiral drugs. However, it should be recognized that the same principles are important for pesticides containing stereogenic centers. A better knowledge of the individual degradation or toxicological data of each enantiomer could reduce the amount of pesticide used, decrease undesired ecological impact, and avoid the unnecessary stereoisomer. Most of triazole pesticides have stereogenic centers that can lead to one or two pairs of enantiomers. These enantiomers can lead to important consequences regarding their bioactivity. For instance, in the case of the triadimenol (**Figure 1**), each enantiomer causes a different biological response (*11*). The biological activity of the *threo* diastereomer is higher than that of the *erythro* diastereomer (*12, 13*). The two enantiomers of a wide range of chiral drugs show differences in terms of bioavailability, distribution, metabolic, and excretion behavior (*14*). Very often, one enantiomer represents the needed activity, while the other one might be active in a different way, contributing to side effects, displaying toxicity, or acting as an antagonist. Nevertheless, most of the triazole pesticides, with the exception of uniconazole and diniconazole, are commercialized as racemic mixtures (*15*). The questions concerning the synthetic method of pure active enantiomers and the influence of stereochemistry upon biological activity for chiral triazole pesticides are therefore of particular interest in this study.

The goal of developing safer and more effective chiral drugs, including medicine and agrochemicals, encouraged us to produce

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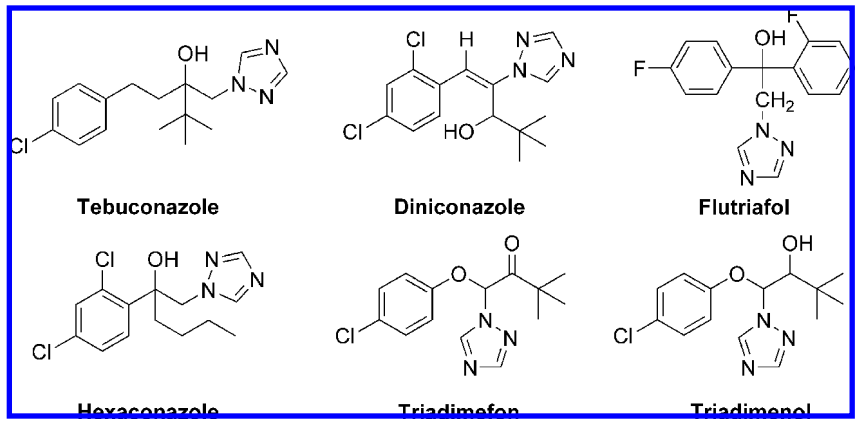
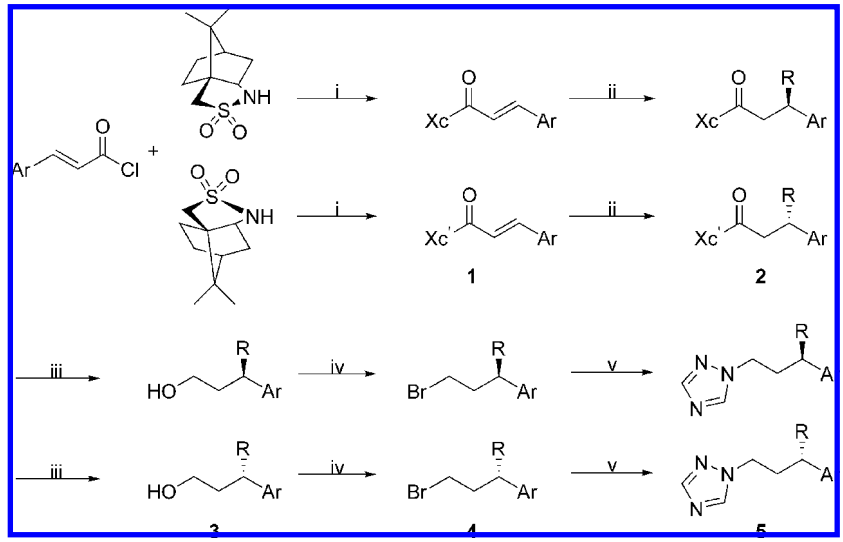


Figure 1. Some representative structures of triazole fungicides containing an asymmetrical carbon atom.

Scheme 1. Synthesis of γ-Aryl-1,2,4-triazole Derivatives **5**[a]



[a] Reagents and conditions: (i) NaH, THF, 24 h. (ii) RMgX, THF, −78 °C. (iii) $NaBH_4$, aqueous THF. (iv) CBr_4, PPh_3, CH_2Cl_2. (v) 1*H*-1,2,4-trizaloe, K_2CO_3, MeCN, reflux, 5−7 h.

pure active enantiomers. As part of our agrochemistry program aimed at researching for active chiral trizole derivatives, we report in this work our effort to design, distereoselectively synthesize, and investigate the in vitro fungicidal activities of novel chiral γ-aryl-1*H*-1,2,4-triazole derivatives. All of the pure 3*R*- and 3*S*-γ-aryl-1*H*-1,2,4-triazole derivatives **5** were obtained conveniently by using the chiral auxiliary (Oppolzer's sultam), as shown in **Scheme 1**, with the high ee value of the triazoles reaching up to 99%. The preliminary in vitro assays showed that compounds **5e**-*R*, **5f**-*R*, **5i**-*R*, **5i**-*S*, and **5j**-*R* have better fungicidal activities at the concentration of 100 μg/mL. The compound **5i**-*R* had a comparably high inhibitory rate and broad spectrum of activity than Bayleton against all of the fungal pathogens tested at the concentration of 50 μg/mL. The structure−activity relationships have been discussed further.

MATERIALS AND METHODS

Chemistry. Unless otherwise noted, all materials were commercially available and were used directly without further purification. All solvents were redistilled before use. *Fusarium oxysporium*, *Rhizoctonia solani*, *Botrytis cinereapers*, *Gibberella zeae*, *Dothiorella gregaria*, and *Colletotrichum gossypii* were provided through the courtesy of the Center for Bioassay, Central China Normal University. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Mercury-Plus 400 spectrometer at 400 or 600 MHz, respectively. The chemical shifts are reported relative to $CDCl_3$ with TMS as the internal reference. MS spectra were determined using a TraceMS 2000 organic mass spectrometer. Elemental analyses were performed on a Vario EL III elemental analysis instrument. Optical rotations were measured on a JASCO P-1010 polarimeter. Melting points were taken on a Buchi B-545 melting point apparatus and were uncorrected.

General Synthetic Procedure for *N*-Enoylsultams 1. The chiral intermediates **1a**−**d** were prepared following the literature methods, and their spectral and analytical data were the same as those given in the literature (*16*−*19*).

General Synthetic Procedure for the Compounds 2. A solution of **1** (10 mmoL) in anhydrous THF (40 mL) under a nitrogen atmosphere was cooled to −78 °C, to which alkylmagnesium bromide (10 mL, 22 mmoL) was added dropwise. The mixture was stirred at −78 °C for 3 h. After completion of the reaction, saturated aqueous NH_4Cl was added, and the organic layer was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to obtain crude product. The crude product was purified by crystallization or by flash chromatography to afford the desired product. The spectral and analytical data of compounds **2a**-*R*, **2b**-*R*, **2c**-*R*, **2e**-*R*, **2f**-*R*, **2h**-*R*, **2i**-*R*, and **2j**-*R* were the same as those in the literature (*20*).

N-[(3S)-3-Phenyl-pentanoyl]bornane-10,2-sultam (**2a**-*S*). White solid; mp 98−100 °C; yield 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, J = 7.6 Hz, 3H), 0.96 (s, 3H), 1.17 (s, 3H), 1.31−1.36 (m, 2H), 1.57−1.69 (m, 2H), 1.87−1.88 (m, 3H), 2.01−2.02(m, 2H), 2.98−3.02 (m, 2H), 3.07−3.12 (m, 1H), 3.40 (d, J = 13.6 Hz, 1H), 3.48 (d, J = 14.0 Hz, 1H), 3.79−3.82 (m, 1H), 7.18−7.21 (m, 3H), 7.27−7.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 19.7, 20.7, 26.2, 29.1, 32.6, 38.3, 41.8, 43.0, 44.4, 47.5, 48.1, 52.8, 65.0, 126.2, 127.5, 128.1, 143.5,

170.4. Anal. calcd for $C_{21}H_{29}NO_3S$: C, 67.17; H, 7.78; N, 3.73; S, 8.54. Found: C, 66.67; H, 7.31; N, 3.53; S, 8.93.

*N-[(3S)-3-(4-Fluorophenyl)pentanoyl]bornane-10,2-sultam (***2b**-*S).* White solid; mp 108−110 °C; yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, J = 7.6 Hz, 3H), 0.96 (s, 3H), 1.15 (s, 3H), 1.31−1.36 (m, 2H), 1.58−1.68 (m, 2H), 1.84−1.89 (m, 3H), 2.01−2.02 (m, 2H), 2.99−3.14 (m, 2H), 3.40 (d, J = 14.0 Hz, 1H), 3.48 (d, J = 13.6 Hz, 1H), 3.78−3.80 (m, 1H), 6.94−6.98 (m, 2H), 7.14−7.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7, 19.6, 20.6, 26.2, 29.1, 32.5, 38.2, 41.8, 42.2, 44.3, 47.5, 48.1, 52.7, 64.9, 114.8, 128.9, 139.1, 161.1, 170.1. Anal. calcd for $C_{21}H_{28}FNO_3S$: C, 64.10; H, 7.17; N, 3.56; S, 8.15. Found: C, 64.36; H, 7.09; N, 3.46; S, 8.37.

*N-[(3S)-3-(4-Chlorophenyl)pentanoyl]bornane-10,2-sultam (***2c**-*S).* White solid; mp 100−102 °C; yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, J = 7.2 Hz, 3H), 0.97 (s, 3H), 1.16 (s, 3H), 1.31−1.34 (m, 2H), 1.65−1.68 (m, 2H), 1.85−1.89 (m, 3H), 2.01−2.02 (m, 2H), 3.01−3.13 (m, 2H), 3.40 (d, J = 14.0 Hz, 1H), 3.49 (d, J = 13.6 Hz, 1H), 3.78−3.81 (m, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 19.7, 20.7, 26.2, 29.1, 32.6, 38.2, 41.5, 43.1, 44.4, 47.5, 48.1, 52.8, 64.9, 128.3, 129.1, 131.8, 141.8, 170.3. Anal. calcd for $C_{21}H_{28}ClNO_3S$: C, 61.52; H, 6.88; N, 3.42; S, 7.82. Found: C, 61.88; H, 7.02; N, 3.36; S, 8.06.

*N-[(3R)-3-(4-Methoxyphenyl)pentanoyl]bornane-10,2-sultam (***2d**-*R).* White solid; mp 130−132 °C; yield 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.76 (t, J = 7.2 Hz, 3H), 0.96 (s, 3H), 1.16 (s, 3H), 1.30−1.36 (m, 2H), 1.63−1.66 (m, 3H), 1.87−1.88 (m, 3H), 2.01−2.02 (m, 2H), 2.97−3.09 (m, 3H), 3.41 (d, J = 14.0 Hz, 1H), 3.45 (d, J = 14.0 Hz, 1H), 3.77 (s, 3H), 3.80−3.82 (m, 1H), 6.81−6.83 (m, 2H), 7.11−7.13 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7, 19.7, 20.7, 26.2, 29.2, 32.6, 38.3, 42.0, 42.3, 44.4, 47.5, 48.1, 52.7, 54.9, 65.0, 113.4, 128.4, 135.6, 157.8, 170.5. Anal. calcd for $C_{22}H_{31}NO_4S$: C, 65.15; H, 7.70; N, 3.45; S, 7.91. Found: C, 64.88; H, 7.62; N, 3.56; S, 8.22.

*N-[(3S)-3-(4-Methoxyphenyl)pentanoyl]bornane-10,2-sultam (***2d**-*S).* Yield 74%. The spectroscopic data were the same as those of **2d**-*R*.

*N-[(3S)-3-Phenyl-hexanoyl]bornane-10,2-sultam (***2e**-*S).* White solid; mp 108−109 °C; yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (t, J = 7.2 Hz, 3H), 0.96 (s, 3H), 1.12 (s, 3H), 1.14−1.20 (m, 1H), 1.30−1.36 (m, 2H), 1.56−1.62 (m, 3H), 1.84−1.88 (m, 3H), 2.01−2.02 (m, 2H), 2.98−3.10 (m, 2H), 3.23−3.26 (m, 1H), 3.40 (d, J = 13.6 Hz, 1H), 3.49 (d, J = 14.0 Hz, 1H), 3.78−3.81 (m, 1H), 7.17−7.21 (m, 3H), 7.26−7.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.7, 20.2, 20.7, 26.2, 32.5, 38.2, 38.4, 41.2, 42.1, 44.4, 47.5, 48.1, 52.7, 64.9, 126.1, 127.4, 128.1, 143.8, 170.4. Anal. calcd for $C_{22}H_{31}NO_3S$: C, 67.83; H, 8.02; N, 3.60; S, 8.23. Found: C, 68.09; H, 8.30; N, 3.55; S, 8.53.

*N-[(3S)-3-(4-Fluorophenyl)hexanoyl]bornane-10,2-sultam (***2f**-*S).* White solid; mp 96−98 °C; yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (t, J = 7.2 Hz, 3H), 0.96 (s, 3H), 1.13−1.14 (m, 2H), 1.15 (s, 3H), 1.30−1.36 (m, 2H), 1.54−1.61 (m, 2H), 1.84−1.88 (m, 3H), 2.0−2.01(m, 2H), 2.98−3.03 (m, 2H), 3.22−3.24 (m, 1H), 3.40 (d, J = 14.0 Hz, 1H), 3.49 (d, J = 13.6 Hz, 1H), 3.77−3.80 (m, 1H), 6.93−6.98 (m, 2H), 7.15−7.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.7, 20.2, 20.7, 26.2, 32.6, 38.2, 38.5, 40.4, 42.1, 44.4, 47.5, 48.1, 52.8, 65.0, 114.9, 128.8, 139.5, 161.2, 170.2. Anal. calcd for $C_{22}H_{30}FNO_3S$: C, 64.84; H, 7.42; N, 3.44; S, 7.87. Found: C, 64.96; H, 7.38; N, 3.42; S, 7.96.

*(3R)-3-(4-Methoxyphenyl)hexanoyl]bornane-10,2-sultam (***2g**-*R).* White solid; mp 108−109 °C; yield 88%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 (t, J = 7.2 Hz, 3H), 0.96 (s, 3H), 1.13−1.18 (m, 5H), 1.31−1.35 (m, 2H), 1.55−1.59 (m, 2H), 1.84−1.88 (m, 3H), 2.0−2.04 (m, 2H), 2.94−3.06 (m, 2H), 3.18−3.19 (m, 1H), 3.40 (d, J = 13.8 Hz, 1H), 3.48 (d, J = 13.8 Hz, 1H), 3.75−3.81 (m, 4H), 6.82 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.7, 20.2, 20.7, 26.2, 32.6, 38.3, 38.6, 40.4, 42.4, 44.4, 47.5, 48.1, 52.8, 54.9, 65.0, 113.5, 128.3, 135.9, 157.7, 170.5. Anal. calcd for $C_{23}H_{33}NO_4S$: C, 65.84; H, 7.93; N, 3.34; S, 7.64; Found: C, 65.96; H, 7.88; N, 3.36; S, 7.87.

*N-[(3S)-3-(4-Methoxyphenyl)hexanoyl]bornane-10,2-sultam (***2g**-*S).* Yield 87%. The spectroscopic data were the same as those of **2g**-*R*.

*N-[(3S)-3-Phenyl-heptanoyl]bornane-10,2-sultam (***2h**-*S).* White solid; mp 63−64 °C; yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, J = 7.2 Hz, 3H), 0.96 (s, 3H), 1.17 (s, 3H), 1.12−1.35 (m, 6H), 1.63−1.65 (m, 2H), 1.86−1.88 (m, 3H), 2.0−2.02 (m, 2H), 3.05−3.07 (m, 2H), 3.21−3.23 (m, 1H), 3.40 (d, J = 14.0 Hz, 1H), 3.48 (d, J = 13.6 Hz, 1H), 3.78−3.81 (m, 1H), 7.18−7.21 (m, 3H), 7.26−7.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.7, 20.7, 22.4, 26.2, 29.2, 32.5, 35.9, 38.2, 41.4, 42.1, 44.3, 47.5, 48.1, 52.7, 64.9, 126.1, 127.4, 128.1, 143.8, 170.4. Anal. calcd for $C_{23}H_{33}NO_3S$: C, 68.45; H, 8.24; N, 3.47; S, 7.95. Found: C, 68.57; H, 8.16; N, 3.31; S, 8.09.

Table 1. ee Value Properties of Compounds **5**

compound	R	Ar	configuration	yield[a]	ee (%)[b]
5a-*R*	Et	Ph	*R*	68	98
5a-*S*	Et	Ph	*S*	75	98
5b-*R*	Et	4-FC_6H_4	*R*	87	82
5b-*S*	Et	4-FC_6H_4	*S*	79	85
5c-*R*	Et	4-ClC_6H_4	*R*	69	84
5c-*S*	Et	4-ClC_6H_4	*S*	80	80
5d-*R*	Et	4-$MeOC_6H_4$	*R*	78	>99
5d-*S*	Et	4-$MeOC_6H_4$	*S*	79	70
5e-*R*	*n*-Pr	Ph	*R*	80	92
5e-*S*	*n*-Pr	Ph	*S*	75	95
5f-*R*	*n*-Pr	4-FC_6H_4	*R*	74	82
5f-*S*	*n*-Pr	4-FC_6H_4	*S*	76	84
5g-*R*	*n*-Pr	4-$MeOC_6H_4$	*R*	73	72
5g-*S*	*n*-Pr	4-$MeOC_6H_4$	*S*	63	86
5h-*R*	*n*-Bu	Ph	*R*	75	80
5h-*S*	*n*-Bu	Ph	*S*	77	88
5i-*R*	*n*-Bu	4-FC_6H_4	*R*	78	86
5i-*S*	*n*-Bu	4-FC_6H_4	*S*	78	84
5j-*R*	*n*-Bu	4-ClC_6H_4	*R*	72	96
5j-*S*	*n*-Bu	4-ClC_6H_4	*S*	74	97

[a] Isolated yields. [b] Determined by HPLC analysis (Chiralcel OJ-H or OD-H).

*N-[(3S)-3-(4-Fluorophenyl)heptanoyl]bornane-10,2-sultam (***2i**-*S).* White solid; mp 93−95 °C; yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.79−0.84 (m, 3H), 0.96 (s, 3H), 1.16 (s, 3H), 1.05−1.38 (m, 6H), 1.54−1.63 (m, 2H), 1.85−1.89 (m, 3H), 2.0−2.01 (m, 2H), 3.0−3.03 (m, 2H), 3.20−3.21 (m, 1H), 3.42 (d, J = 13.6 Hz, 1H), 3.49 (d, J = 13.6 Hz, 1H), 3.78−3.81 (m, 1H), 6.93−6.98 (m, 2H), 7.15−7.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.7, 20.7, 22.4, 26.2, 29.2, 32.6, 36.1, 38.2, 40.7, 42.2, 44.4, 47.5, 48.1, 52.8, 65.0, 114.8, 129.0, 139.5, 161.2, 170.2. Anal. calcd for $C_{23}H_{32}FNO_3S$: C, 65.53; H, 7.65; N, 3.32; S, 7.61. Found: C, 65.46; H, 7.66; N, 3.22; S, 7.95.

*N-[(3S)-3-(4-Chlorophenyl)heptanoyl]bornane-10,2-sultam (***2j**-*S).* White solid; mp 116−117 °C; yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, J = 7.2 Hz, 3H), 0.96 (s, 3H), 1.15 (s, 3H), 1.05−1.39 (m, 6H), 1.54−1.63 (m, 2H), 1.85−1.89 (m, 3H), 2.0−2.01 (m, 2H), 3.0−3.03 (m, 2H), 3.18−3.20 (m, 1H), 3.41 (d, J = 13.6 Hz, 1H), 3.49 (d, J = 13.6 Hz, 1H), 3.77−3.80 (m, 1H), 7.14 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.7, 20.6, 22.3, 26.2, 29.1, 32.5, 35.9, 38.2, 40.7, 41.9, 44.4, 47.5, 48.1, 52.7, 64.9, 128.2, 128.8, 131.6, 142.4, 170.0. Anal. calcd for $C_{23}H_{32}ClNO_3S$: C, 63.07; H, 7.36; N, 3.20; S, 7.32. Found: C, 63.32; H, 7.42; N, 3.17; S, 7.52.

General Synthetic Procedure for the Compounds 3. A solution of sodium borohydride (40 mmol; 4 equivalents) in water (10 mL) was added dropwise to a cooled (ice water) solution of **2** (10 mmol) in THF (30 mL). The mixture was stirred at room temperature, and the completion of the reaction was monitored by TLC. To the reaction mixture was added 2 mol/L HCl at a rate to maintain the internal temperature at 20−25 °C. The reaction mixture was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with brine (50 mL), concentrated, and purified by silica gel chromatography to obtain the desired products. The spectral and analytical data of compounds **3a**-*R* (*21*), **3b**-*R*, **3c**-*R*, **3e**-*R*, **3f**-*R*, **3h**-*R* (*22*−*24*), **3i**-*R*, and **3j**-*R* were the same as those given in the literature (*22*−*24*).

*(3S)-3-Phenylpentan-1-ol (***3a**-*S).* Colorless oil; yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.78 (t, J = 7.6 Hz, 3H), 1.12 (s, 1H), 1.56−1.59 (m, 1H), 1.61−1.71 (m, 1H), 1.79−1.83 (m, 1H), 1.94−1.98 (m, 1H), 2.57−2.61 (m, 1H), 3.48−3.53 (m, 2H), 7.15−7.21 (m, 3H), 7.23−7.31 (m, 2H). Anal. calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.28;

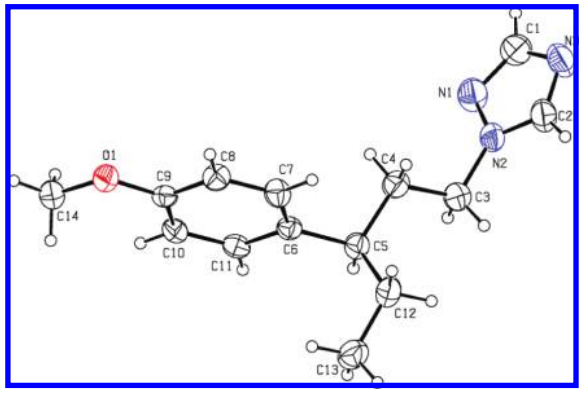


Figure 2. Molecular structure of compound **5d**-*R*.

H, 9.98. All spectroscopic data were in agreement with those reported in the literature (*25, 26*).

*(3S)-3-(4-Fluorophenyl)pentan-1-ol (***3b***-S).* Colorless oil; yield 88%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.77 (t, J = 7.2 Hz, 3H), 1.16 (s, 1H), 1.56−1.60 (m, 1H), 1.67−1.68 (m, 1H), 1.74−1.77 (m, 1H), 1.94−1.95 (m, 1H), 2.59−2.60 (m, 1H), 3.45 (s, 1H), 3.53 (s, 1H), 6.97−7.00 (m, 2H), 7.10−7.12 (m, 2H). Anal. calcd for $C_{11}H_{15}FO$: C, 72.50; H, 8.30. Found: C, 72.34; H, 8.58.

*(3S)-3-(4-Chlorophenyl)pentan-1-ol (***3c***-S).* Colorless oil; yield 90%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.77 (t, J = 7.2 Hz, 3H), 1.22 (s, 1H), 1.55−1.56 (m, 1H), 1.67−1.69 (m, 1H), 1.75−1.77 (m, 1H), 1.92−1.96 (m, 1H), 2.59−2.60 (m, 1H), 3.43−3.45 (m, 1H), 3.52−3.54 (m, 1H), 7.10 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H). Anal. calcd for $C_{11}H_{15}ClO$: C, 66.49; H, 7.61. Found: C, 66.21; H, 7.56. All spectroscopic data were in agreement with those reported in the literature (*27*).

*(3R)-3-(4-Methoxyphenyl)pentan-1-ol (***3d***-R).* Colorless oil; yield 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, J = 7.2 Hz, 3H), 1.32 (s, 1H), 1.50−1.79 (m, 3H), 1.88−1.95 (m, 1H), 2.51−2.55 (m, 1H), 3.42−3.55 (m, 2H), 3.78 (s, 3H), 6.84 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H). Anal. calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.98; H, 9.38. All spectroscopic data were in agreement with those reported in the literature (*27*).

*(3S)-3-(4-Methoxyphenyl)pentan-1-ol (***3d***-S).* Colorless oil; yield 90%. The spectroscopic data were the same as those of **3d**-*R*.

*(3S)-3-Phenylhexan-1-ol (***3e***-S).* Colorless oil; yield 92%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 (t, J = 7.2 Hz, 3H), 1.14−1.19 (m, 3H), 1.57−1.61 (m, 2H), 1.80−1.81 (m, 1H), 1.92−1.93 (m, 1H), 2.69−2.70 (m, 1H), 3.45−3.46 (m, 1H), 3.52−3.53 (m, 1H), 7.16−7.20 (m, 3H), 7.26−7.30 (m, 2H). Anal. calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.68; H, 9.98. All spectroscopic data were in agreement with those reported in the literature (*28, 29*).

*(3S)-3-(4-Fluorophenyl)hexan-1-ol (***3f***-S).* Colorless oil; yield 89%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 (t, J = 7.2 Hz, 3H), 1.13−1.18 (m, 3H), 1.52−1.62 (m, 2H), 1.74−1.76 (m, 1H), 1.91−1.93 (m, 1H), 2.70−2.71 (m, 1H), 3.43−3.44 (m, 1H), 3.52−3.53 (m, 1H), 6.96−7.0 (t, J = 8.4 Hz, 2H), 7.10−7.13 (m, 2H). Anal. calcd for $C_{12}H_{17}FO$: C, 73.44; H, 8.73; Anal. calcd for $C_{12}H_{17}FO$: C, 73.44; H, 8.73. Found: C, 73.18; H, 8.47.

*(3R)-3-(4-Methoxyphenyl)hexan-1-ol (***3g***-R).* Colorless oil; yield 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (t, J = 7.2 Hz, 3H), 1.12−1.15 (m, 2H), 1.27 (s, 1H), 1.53−1.57 (m, 2H), 1.73−1.75 (m, 1H), 1.88−1.91 (m, 1H), 2.64 (m, 1H), 3.44−3.50 (m, 2H), 3.78 (s, 3H), 6.83 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H). Anal. calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.85; H, 9.81.

*(3S)-3-(4-Methoxyphenyl)hexan-1-ol (***3g***-S).* Colorless oil; yield 88%. The spectroscopic data were the same as those of **3g**-*R*.

*(S)-3-Phenylheptan-1-ol (***3h***-S).* Colorless oil; yield 93%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.83 (t, J = 7.2 Hz, 3H), 1.08−1.18 (m, 3H), 1.20−1.29 (m, 2H), 1.60−1.65 (m, 2H), 1.78−1.82 (m, 1H), 1.93−1.96 (m, 1H), 2.66−2.69 (m, 1H), 3.46−3.47 (m, 1H), 3.52−3.53 (m, 1H), 7.16−7.21 (m, 3H), 7.26−7.30 (m, 2H). Anal. calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.05; H, 10.61. All spectroscopic data were in agreement with those reported in the literature (*30*).

*(3S)-3-(4-Fluorophenyl)heptan-1-ol (***3i***-S).* Colorless oil; yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82 (t, J = 7.2 Hz, 3H), 1.05−1.29 (m, 5H), 1.51−1.64 (m, 2H), 1.73−1.77 (m, 1H), 1.90−1.93 (m, 1H), 2.65−2.69 (m, 1H), 3.44−3.52 (m, 2H), 6.95−7.0 (m, 2H), 7.09−7.13 (m, 2H). Anal. calcd for $C_{13}H_{19}FO$: C, 74.25; H, 9.11. Found: C, 74.33; H, 9.37.

*(3S)-3-(4-Chlorophenyl)heptan-1-ol (***3j***-S).* Colorless oil; yield 90%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.82 (t, J = 7.2 Hz, 3H), 1.08−1.28 (m, 5H), 1.53−1.62 (m, 2H), 1.74−1.75 (m, 1H), 1.91−1.93 (m, 1H), 2.67−2.68 (m, 1H), 3.43−3.44 (m, 1H), 3.51−3.52 (m, 1H), 7.10 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H). Anal. calcd for $C_{13}H_{19}ClO$: C, 68.86; H, 8.45. Found: C, 68.72; H, 8.63.

General Synthetic Procedure for the Compounds 4. A solution of (0.027 mmoL) triphenylphosphine in methylene chloride (15 mL) was added dropwise to a cooled (ice water) methylene chloride (10 mL) solution of **3** (0.01moL) and carbon tetrabromide (0.027 moL). The mixture was stirred 10−15 h at room temperature. After completion of the reaction, the solution was filtered to remove the triphenylphosphine oxide. The filtrate was evaporated under reduced pressure to give crude product. The crude product was purified by column chromatography to give pure product as a colorless oil.

*(3R)-3-Phenyl-1-bromopentane (***4a***-R).* Colorless oil; yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80 (t, J = 7.2 Hz, 3H), 1.60−1.71 (m, 2H), 2.08−2.22 (m, 2H), 2.64−2.69 (m, 1H), 3.08−3.15 (m, 1H), 3.26−3.32 (m, 1H), 7.16−7.33 (m, 5H). All spectroscopic data were in agreement with those reported in the literature (*31, 32*).

*(3S)-3-Phenyl-1-bromopentane (***4a***-S).* Colorless oil; yield 83%. The spectroscopic data were the same as those of **4a**-*R*.

*(3R)-3-(4-Fluorophenyl)-1-bromopentane (***4b***-R).* Colorless oil; yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.78 (t, J = 7.2 Hz, 3H), 1.55−1.70 (m, 2H), 2.02−2.07 (m, 1H), 2.15−2.18 (m, 1H), 2.66−2.69 (m, 1H), 3.07−3.10 (m, 1H), 3.26−3.32 (m, 1H), 7.0 (t, J = 8.4 Hz, 2H), 7.10−7.14 (m, 2H).

*(3S)-3-(4-Fluorophenyl)-1-bromopentane (***4b***-S).* Colorless oil; yield 90%. The spectroscopic data were the same as those of **4b**-*R*.

*(3R)-3-(4-Chlorophenyl)-1-bromopentane (***4c***-R).* Colorless oil; yield 76%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.78 (t, J = 7.2 Hz, 3H), 1.55−1.70 (m, 2H), 2.01−2.05 (m, 1H), 2.15−2.18 (m, 1H), 2.66−2.69 (m, 1H), 3.05−3.09 (m, 1H), 3.27−3.31 (m, 1H), 7.11 (d, J = 8.4 Hz, 2H), 7.25−7.29 (m, 2H).

*(3S)-3-(4-Chlorophenyl)-1-bromopentane (***4c***-S).* Colorless oil; yield 71%. The spectroscopic data were the same as those of **4c**-*R*.

*(3R)-3-(4-Methoxyphenyl)-1-bromopentane (***4d***-R).* Colorless oil; yield 82%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.78 (t, J = 7.2 Hz, 3H), 1.55−1.59 (m, 1H), 1.64−1.67 (m, 1H), 2.0−2.05 (m, 1H), 2.14−2.17 (m, 1H), 2.60−2.63 (m, 1H), 3.08−3.11 (m, 1H), 3.27−3.30 (m, 1H), 3.81 (s, 3H), 6.85 (d, J = 6.6 Hz, 2H), 7.07 (d, J = 7.2 Hz, 2H).

*(3S)-3-(4-Methoxyphenyl)-1-bromopentane (***4d***-S).* Colorless oil; yield 78%. The spectroscopic data were the same as those of **4d**-*R*.

*(3R)-3-Phenyl-1-bromohexane (***4e***-R).* Colorless oil; yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, J = 7.2 Hz, 3H), 1.14−1.22 (m, 2H), 1.55−1.63 (m, 2H), 2.07−2.17 (m, 2H), 2.77 (m, 1H), 3.09−3.13 (m, 1H), 3.25−3.29 (m, 1H), 7.15−7.22 (m, 2H), 7.28−7.32 (m, 3H). All spectroscopic data were in agreement with those reported in the literature (*33*).

*(3S)-3-Phenyl-1-bromohexane (***4e***-S).* Colorless oil; yield 89%. The spectroscopic data were the same as those of **4e**-*R*.

*(3R)-3-(4-Fluorophenyl)-1-bromohexane (***4f***-R).* Colorless oil; yield 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, J = 7.2 Hz, 3H), 1.12−1.20 (m, 2H), 1.53−1.61 (m, 2H), 2.01−2.16 (m, 2H), 2.76−2.79 (m, 1H), 3.03−3.09 (m, 1H), 3.26−3.31 (m, 1H), 6.97−7.01 (m, 2H), 7.11−7.14 (m, 2H).

*(3S)-3-(4-Fluorophenyl)-1-bromohexane (***4f***-S).* Colorless oil; yield 85%. The spectroscopic data were the same as those of **4f**-*R*.

*(3R)-3-(4-Methoxyphenyl)-1-bromohexane (***4g***-R).* Colorless oil; yield 89%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.85 (t, J = 7.2 Hz, 3H), 1.14−1.20 (m, 2H), 1.54−1.58 (m, 2H), 2.0−2.04 (m, 1H), 2.12−2.17 (m, 1H), 2.71−2.73 (m, 1H), 3.07−3.11 (m, 1H), 3.26−3.30 (m, 1H), 3.80 (s, 3H), 6.85 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H).

*(3S)-3-(4-Methoxyphenyl)-1-bromohexane (***4g***-S).* Colorless oil; yield 90%. The spectroscopic data were the same as those of **4g**-*R*.

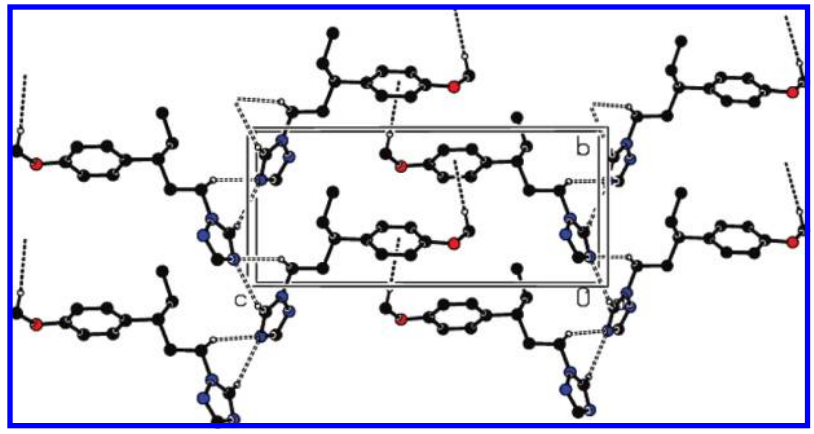


Figure 3. Packing diagram of the unit cell of compound **5d**-*R*.

Table 2. In Vitro Fungicidal Activities of Compounds **5a**−**j** (100 mg L^{-1}, Inhibitory Rate Percent)[a]

				inhibitory rate (%)					
compound	R	Ar	configuration	*F. oxysporium*	*R. solani*	*B. cinereapers*	*G. zeae*	*D. gregaria*	*C. gossypii*
5a-*R*	Et	Ph	*R*	60 ± 2	80 ± 3	52 ± 3	60 ± 2	81 ± 2	70 ± 2
5a-*S*	Et	Ph	*S*	55 ± 3	75 ± 3	52 ± 4	63 ± 2	60 ± 3	50 ± 3
5b-*R*	Et	4-FC_6H_4	*R*	50 ± 2	82 ± 2	36 ± 5	63 ± 3	82 ± 2	78 ± 2
5b-*S*	Et	4-FC_6H_4	*S*	60 ± 3	85 ± 2	52 ± 4	56 ± 3	75 ± 2	65 ± 3
5c-*R*	Et	4-ClC_6H_4	*R*	91 ± 2	85 ± 2	94 ± 2	76 ± 2	93 ± 1	97 ± 1
5c-*S*	Et	4-ClC_6H_4	*S*	80 ± 1	83 ± 2	84 ± 3	73 ± 3	80 ± 2	85 ± 2
5d-*R*	Et	4-$MeOC_6H_4$	*R*	65 ± 3	60 ± 4	30 ± 5	66 ± 3	82 ± 2	55 ± 4
5d-*S*	Et	4-$MeOC_6H_4$	*S*	40 ± 3	73 ± 3	30 ± 5	42 ± 4	45 ± 4	50 ± 5
5e-*R*	*n*-Pr	Ph	*R*	80 ± 2	97 ± 1	98 ± 1	83 ± 3	100 ± 1	92 ± 1
5e-*S*	*n*-Pr	Ph	*S*	55 ± 3	78 ± 2	44 ± 4	52 ± 3	67 ± 2	75 ± 2
5f-*R*	*n*-Pr	4-FC_6H_4	*R*	82 ± 1	90 ± 2	71 ± 3	85 ± 2	100 ± 1	95 ± 1
5f-*S*	*n*-Pr	4-FC_6H_4	*S*	73 ± 2	86 ± 3	94 ± 2	83 ± 2	83 ± 2	90 ± 2
5g-*R*	*n*-Pr	4-$MeOC_6H_4$	*R*	90 ± 1	78 ± 2	60 ± 3	66 ± 3	90 ± 2	80 ± 3
5g-*S*	*n*-Pr	4-$MeOC_6H_4$	*S*	75 ± 2	90 ± 3	92 ± 1	76 ± 2	93 ± 1	90 ± 2
5h-*R*	*n*-Bu	Ph	*R*	66 ± 3	90 ± 3	91 ± 2	71 ± 3	100 ± 1	87 ± 2
5h-*S*	*n*-Bu	Ph	*S*	74 ± 3	87 ± 2	91 ± 1	71 ± 3	96 ± 1	82 ± 2
5i-*R*	*n*-Bu	4-FC_6H_4	*R*	100 ± 1	100 ± 1	100 ± 1	95 ± 1	100 ± 1	100 ± 1
5i-*S*	*n*-Bu	4-FC_6H_4	*S*	96 ± 1	100 ± 1	96 ± 1	83 ± 2	97 ± 1	95 ± 1
5j-*R*	*n*-Bu	4-ClC_6H_4	*R*	82 ± 2	91 ± 1	88 ± 2	73 ± 3	100 ± 0	85 ± 2
5j-*S*	*n*-Bu	4-ClC_6H_4	*S*	78 ± 2	84 ± 2	94 ± 1	69 ± 3	97 ± 1	85 ± 2
bayleton				97 ± 1	100 ± 1	96 ± 1	76 ± 2	71 ± 3	100 ± 1

[a] The mean value for relative inhibition was calculated from at least three determinations.

*(3R)-3-Phenyl-1-bromoheptane (***4h**-*R).* Colorless oil; yield 91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82 (t, J = 7.2 Hz, 3H), 1.04−1.31 (m, 4H), 1.55−1.65 (m, 2H), 2.03−2.20 (m, 2H), 2.71−2.78 (m, 1H), 3.06−3.13 (m, 1H), 3.24−3.28 (m, 1H), 7.15−7.31 (m, 5H). All spectroscopic data were in agreement with those reported in the literature (*34*).

*(3S)-3-Phenyl-1-bromoheptane (***4h**-*S).* Colorless oil; yield 85%. The spectroscopic data were the same as those of **4h**-*R*.

*(3R)-3-(4-Fluorophenyl)-1-bromoheptane (***4i**-*R).* Colorless oil; yield 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (t, J = 7.8 Hz, 3H), 1.09−1.28 (m, 4H), 1.55−1.64 (m, 2H), 2.03−2.04 (m, 1H), 2.15−2.17 (m, 1H), 2.74−2.77 (m, 1H), 3.05−3.10 (m, 1H), 3.27−3.30 (m, 1H), 6.97−7.01 (m, 2H), 7.10−7.14 (m, 2H).

*(3S)-3-(4-Fluorophenyl)-1-bromoheptane (***4i**-*S).* Colorless oil; yield 88%. The spectroscopic data were the same as those of **4i**-*R*.

*(3R)-3-(4-Chlorophenyl)-1-bromoheptane (***4j**-*R).* Colorless oil; yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (t, J = 7.6 Hz, 3H), 1.09−1.28 (m, 4H), 1.54−1.62 (m, 2H), 2.01−2.03 (m, 1H), 2.15−2.16 (m, 1H), 2.74−2.77 (m, 1H), 3.03−3.09 (m, 1H), 3.25−3.29 (m, 1H), 7.09−7.11 (m, 2H), 7.27−7.29 (m, 2H).

*(3S)-3-(4-Chlorophenyl)-1-bromoheptane (***4j**-*S).* Colorless oil; yield 86%. The spectroscopic data were the same as those of **4j**-*R*.

General Procedure for the Synthesis of the Title Compounds 5. A mixture of **4** (0.05 mmol), K_2CO_3 (0.25 mmol), and 1*H*-1,2,4-triazole (0.06 mmol) in CH_3CN (25 mL) was stirred at 60−70 °C for 5−7 h. After completion of the reaction, the reaction mixture was cooled to room temperature and filtered. The filtrate was washed with water (5 mL), dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure to give crude product. The crude product was purified by column chromatography to give compounds **5**.

*1-[(3R)-3-Phenylpentyl]-1H-1,2,4-triazole (***5a**-*R).* Colorless oil; yield 68%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, J = 7.2 Hz, 3H), 1.58−1.68 (m, 2H), 2.07−2.09 (m, 1H), 2.30−2.39 (m, 2H), 3.93−4.0 (m, 2H), 7.12−7.13 (m, 2H), 7.23−7.24 (m, 1H), 7.29−7.35 (m, 2H), 7.89 (s, 1H), 7.96 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.9, 29.9, 35.6, 44.7, 47.7, 126.6, 127.5, 128.6, 143.2, 152.0. MS: *m*/*z*: 215. Anal. calcd for $C_{13}H_{17}N_3$: C, 72.52; H, 7.96; N, 19.52. Found: C, 72.38; H, 7.86; N, 19.76; $[\alpha]_D^{23}$ = −14.0 (*c* 1.0, CH_2Cl_2); 98% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OJ-H column (hexane/2-propanol = 90/10, 1 mL/min), t_{minor} = 24.90 min, t_{major} =33.59 min.

*1-[(3S)-3-Phenylpentyl]-1H-1,2,4-triazole (***5a**-*S).* Colorless oil; yield 75%; $[\alpha]_D^{23}$ = 23.3 (*c* 1.0, CH_2Cl_2); 98% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OJ-H column (hexane/2-propanol = 90/10, 1 mL/min), t_{major} = 23.53 min, t_{minor} = 35.04 min. The spectroscopic data were the same as those of **5a**-*R*.

*1-[(3R)-3-(4-Fluorophenyl)pentyl]-1H-1,2,4-triazole (***5b**-*R).* Colorless oil; yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.75 (t, J = 6.8 Hz, 3H), 1.54−1.59 (m, 1H), 1.65−1.71 (m, 1H), 2.01 (m, 1H), 2.32−2.39 (m, 2H), 3.95−4.02 (m, 2H), 7.01−7.11 (m, 4H), 7.96 (s, 1H), 8.03 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 29.6, 35.9, 44.0, 47.9, 115.4, 115.6, 128.9, 128.9, 138.9, 152.1. MS: *m*/*z*: 233. Anal. calcd for $C_{13}H_{16}FN_3$: C, 66.93; H, 6.91; N, 18.01. Found: C, 66.78; H, 6.98;

Table 3. In Vitro Fungicidal Activities of Compounds **5i**-*R* and **5i**-*S* Comparison with Bayleton (50 mg L^{-1}, Inhibitory Rate Percent)[a]

				inhibitory rate (%)					
compound	R	Ar	configuration	*F. oxysporum*	*R. solani*	*B. cinereapers*	*G. zeae*	*D. gregaria*	*C. gossypii*
5i-*R*	*n*-Bu	4-FC_6H_4	*R*	99 ± 1	99 ± 1	100 ± 1	89 ± 2	100 ± 1	100 ± 1
5i-*S*	*n*-Bu	4-FC_6H_4	*S*	88 ± 2	88 ± 1	81 ± 2	70 ± 3	71 ± 3	85 ± 2
bayleton				91 ± 1	91 ± 1	78 ± 2	59 ± 2	14 ± 3	97 ± 1

[a] The mean value for relative inhibition was calculated from at least three determinations.

Table 4. In Vitro Fungicidal Activities of Compounds **5i**-*R* and **5i**-*S* Comparison with Bayleton Expressed as 50% Effective Concentration (EC_{50}, mM)[a]

			EC_{50} (mM)					
compound	R	Ar	*F. oxysporum*	*R. solani*	*B. cinereapers*	*G. zeae*	*D. gregaria*	*C. gossypii*
5i-*R*	*n*-Bu	4-FC_6H_4	0.112 ± 0.002	0.036 ± 0.005	0.061 ± 0.001	0.066 ± 0.005	0.015 ± 0.004	0.061 ± 0.001
5i-*S*	*n*-Bu	4-FC_6H_4	0.109 ± 0.003	0.049 ± 0.001	0.056 ± 0.004	0.104 ± 0.004	0.079 ± 0.001	0.063 ± 0.003
bayleton			0.040 ± 0.004	0.014 ± 0.004	0.041 ± 0.001	0.163 ± 0.003	0.317 ± 0.003	0.019 ± 0.001

[a] The mean value for relative inhibition was calculated from at least three determinations.

N, 17.96. $[\alpha]_D^{23} = -10.9$ (*c* 0.99, CH_2Cl_2); 82% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 9.80$ min, $t_{major} = 14.02$ min.

*1-[(3S)-3-(4-Fluorophenyl)pentyl]-1H-1,2,4-triazole (***5b***-S).* Colorless oil; yield 79%; $[\alpha]_D^{23} = 17.1$ (*c* 0.98, CH_2Cl_2); 85% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 9.75$ min, $t_{minor} = 13.84$ min. The spectroscopic data were the same as those of **5b**-*R*.

*1-[(3R)-3-(4-Chlorophenyl)pentyl]-1H-1,2,4-triazole (***5c***-R).* Colorless oil; yield 69%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (t, $J = 7.2$ Hz, 3H), 1.54−1.59 (m, 1H), 1.64−1.69 (m, 1H), 2.03−2.09 (m, 1H), 2.29−2.38 (m, 2H), 3.90−4.02 (m, 2H), 7.07 (d, $J = 8.4$ Hz, 2H), 7.31 (d, $J = 8.4$ Hz, 2H), 7.89 (s, 1H), 7.95 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.8, 29.8, 35.7, 44.1, 47.6, 128.8, 128.9, 132.2, 141.7, 142.9, 151.9. MS: *m/z*: 249. Anal. calcd for $C_{13}H_{16}ClN_3$: C, 62.52; H, 6.46; N, 16.83. Found: C, 62.38; H, 6.52; N, 16.92; $[\alpha]_D^{22} = -16.8$ (*c* 0.99, CH_2Cl_2); 84% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 17.75$ min, $t_{minor} = 24.69$ min.

*1-[(3S)-3-(4-Chlorophenyl)pentyl]-1H-1,2,4-triazole (***5c***-S).* Colorless oil; yield 80%; $[\alpha]_D^{22} = 23.8$ (*c* 1.0, CH_2Cl_2); 80% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 17.32$ min, $t_{major} = 24.32$ min. The spectroscopic data were the same as those of **5c**-*R*.

*1-[(3R)-3-(4-Methoxyphenyl)pentyl]-1H-1,2,4-triazole (***5d***-R).* White solid; yield 78%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.74 (t, $J = 7.2$ Hz, 3H), 1.54−1.56 (m, 1H), 1.63−1.65 (m, 1H), 2.02−2.03 (m, 1H), 2.26−2.33 (m, 2H), 3.79 (s, 3H), 3.91−3.97 (m, 2H), 6.86 (d, $J = 7.2$ Hz, 2H), 7.03 (d, $J = 6.6$ Hz, 2H), 7.85 (s, 1H), 7.92 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.9, 30.0, 35.8, 43.7, 47.7, 55.1, 113.9, 128.4, 135.0, 142.9, 151.8. MS: *m/z*: 245. Anal. calcd for $C_{14}H_{19}N_3O$: C, 68.54; H, 7.81; N, 17.13. Found: C, 68.17; H, 7.92; N, 17.28. $[\alpha]_D^{22} = -16.2$ (*c* 1.0, CH_2Cl_2); 99.3% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 19.77$ min, $t_{minor} = 26.65$ min.

*1-[(3S)-3-(4-Methoxyphenyl)pentyl]-1H-1,2,4-triazole (***5d***-S).* White solid; yield 79%; $[\alpha]_D^{22} = 22.3$ (*c* 0.5, CH_2Cl_2); 71% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 19.22$ min, $t_{major} = 27.27$ min. The spectroscopic data were the same as those of **5d**-*R*.

*1-[(3R)-3-Phenylhexyl]-1H-1,2,4-triazole (***5e***-R).* Colorless oil; yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, $J = 7.2$ Hz, 3H), 1.1−1.18 (m, 2H), 1.56−1.61 (m, 2H), 2.06−2.1 (m, 1H), 2.32−2.36 (m, 1H), 2.42−2.45 (m, 1H), 3.9−3.98 (m, 2H), 7.13 (d, $J = 8$ Hz, 2H), 7.22−7.27 (m, 1H), 7.31−7.35 (m, 2H), 7.84 (s, 1H), 7.93 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 20.3, 35.9, 39.1, 42.6, 47.7, 126.5, 127.4, 128.6, 142.9, 143.5, 151.8. MS: *m/z*: 229. Anal. calcd for $C_{14}H_{19}N_3$: C, 73.33; H, 8.35; N, 18.32. Found: C, 73.18; H, 8.42; N, 18.40. $[\alpha]_D^{20} = -17.1$ (*c* 0.98, CH_2Cl_2); 92% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 16.33$ min, $t_{major} = 24.24$ min.

*1-[(3S)-3-Phenylhexyl]-1H-1,2,4-triazole (***5e***-S).* Colorless oil; yield 75%; $[\alpha]_D^{20} = 16.9$ (*c* 0.99, CH_2Cl_2); 95% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 15.17$ min, $t_{minor} = 18.46$ min. The spectroscopic data were the same as those of **5e**-*R*.

*1-[(3R)-3-(4-Fluorophenyl)hexyl]-1H-1,2,4-triazole (***5f***-R).* Colorless oil; yield 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, $J = 7.2$ Hz, 3H), 1.08−1.15 (m, 2H), 1.52−1.60 (m, 2H), 2.03−2.07 (m, 1H), 2.31−2.36 (m, 1H), 2.42−2.46 (m, 1H), 3.91−3.99 (m, 2H), 6.99−7.04 (m, 2H), 7.07−7.12 (m, 2H), 7.89 (s, 1H), 7.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 20.2, 36.0, 39.1, 41.7, 47.4, 115.1, 115.3, 128.7, 139.0, 142.7, 142.9, 151.6, 151.8. MS: *m/z*: 248 (M + 1). Anal. calcd for $C_{14}H_{18}FN_3$: C, 67.99; H, 7.34; N, 16.99. Found: C, 67.68; H, 7.44; N, 17.06. $[\alpha]_D^{22} = -11.5$ (*c* 0.99, CH_2Cl_2); 82% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 9.62$ min, $t_{minor} = 12.69$ min.

*1-[(3S)-3-(4-Fluorophenyl)hexyl]-1H-1,2,4-triazole (***5f***-S).* Colorless oil; yield 76%; $[\alpha]_D^{22} = 15.4$ (*c* 1.0, CH_2Cl_2); 84% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 9.56$ min, $t_{major} = 12.64$ min. The spectroscopic data were the same as those of **5f**-*R*.

*1-[(3R)-3-(4-Methoxyphenyl)hexyl]-1H-1,2,4-triazole (***5g***-R).* Colorless oil; yield 73%. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.82 (t, $J = 7.2$ Hz, 3H), 1.10−1.16 (m, 2H), 1.52−1.57 (m, 2H), 2.01−2.03 (m, 1H), 2.30−2.39 (m, 2H), 3.80 (t, $J = 9.6$ Hz, 3H), 3.9−3.99 (m, 2H), 6.87 (d, $J = 8.4$ Hz, 2H), 7.04 (d, $J = 8.4$ Hz, 2H), 7.86 (s, 1H), 7.93 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 20.3, 36.0, 39.3, 41.6, 47.6, 55.1, 113.8, 114.0, 128.2, 128.4, 135.3, 142.8, 151.8. MS: *m/z*: 258 (M − 1). Anal. calcd for $C_{15}H_{21}N_3O$: C, 69.47; H, 8.16; N, 16.20. Found: C, 69.07; H, 8.19; N, 16.32. $[\alpha]_D^{20} = -12.5$ (*c* 1.0, CH_2Cl_2); 72% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 31.45$ min, $t_{minor} = 74.06$ min.

*1-[(3S)-3-(4-Methoxyphenyl)hexyl]-1H-1,2,4-triazole (***5g***-S).* Colorless oil; yield 63%; $[\alpha]_D^{20} = 15.6$ (*c* 0.49, CH_2Cl_2); 86% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 28.76$ min, $t_{major} = 80.41$ min. The spectroscopic data were the same as those of **5g**-*R*.

*1-[(3R)-3-Phenylheptyl]-1H-1,2,4-triazole (***5h***-R).* Colorless oil; yield 75%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, $J = 7.2$ Hz, 3H), 1.04−1.27 (m, 4H), 1.57−1.64 (m, 2H), 2.07−2.09 (m, 1H), 2.33−2.42 (m, 2H), 3.92−3.98 (m, 2H), 7.13 (d, $J = 7.2$ Hz, 2H), 7.23 (m, 1H), 7.33 (m, 2H), 7.85 (s, 1H), 7.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 22.4, 29.3, 35.9, 36.6, 42.9, 47.7, 126.5, 127.4, 128.6, 142.8, 143.5, 151.7. MS: *m/z*: 243, 244 (M + 1). Anal. calcd for $C_{15}H_{21}N_3$: C, 74.03; H, 8.70; N, 17.27. Found: C, 73.86; H, 8.81; N, 17.33. $[\alpha]_D^{22} = -15.9$ (*c* 0.51, CH_2Cl_2); 80% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 18.92$ min, $t_{major} = 22.33$ min.

*1-[(3S)-3-Phenylheptyl]-1H-1,2,4-triazole (***5h***-S).* Colorless oil; yield 77%; $[\alpha]_D^{22} = 14.5$ (*c* 0.99, CH_2Cl_2); 88% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 18.58$ min, $t_{minor} = 20.95$ min. The spectroscopic data were the same as those of **5h**-*R*.

*1-[(3R)-3-(4-Fluorophenyl)heptyl]-1H-1,2,4-triazole (***5i***-R).* Colorless oil; yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, $J = 7.2$ Hz, 3H), 1.02−1.27 (m, 4H), 1.53−1.63 (m, 2H), 2.02−2.05 (m, 1H), 2.31−2.42 (m, 2H), 3.91−3.98 (m, 2H), 7.0−7.04 (m, 2H), 7.07−7.11 (m, 2H), 7.87 (s, 1H), 7.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 22.3, 29.2, 36.0, 36.6, 42.0, 42.1, 47.5, 47.6, 115.3, 128.6, 128.7, 139.1, 142.7, 151.6, 151.8. MS: *m*/*z*: 261, 262 (M + 1). Anal. calcd for $C_{15}H_{20}FN_3$: C, 68.94; H, 7.71; N, 16.08. Found: C, 68.48; H, 7.60; N, 15.86. $[\alpha]_D^{22} = -5.6$ (*c* 1.0, CH_2Cl_2); 87% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 8.05$ min, $t_{minor} = 11.16$ min.

*1-[(3S)-3-(4-Fluorophenyl)heptyl]-1H-1,2,4-triazole (***5i***-S).* Colorless oil; yield 78%; $[\alpha]_D^{22} = 9.9$ (*c* 0.99, CH_2Cl_2); 84% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 8.03$ min, $t_{major} = 11.11$ min. The spectroscopic data were the same as those of **5i**-*R*.

*1-[(3R)-3-(4-Chlorophenyl)heptyl]-1H-1,2,4-triazole (***5j***-R).* Colorless oil; yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (t, $J = 7.2$ Hz, 3H), 1.04−1.25 (m, 4H), 1.55−1.63 (m, 2H), 2.05 (m, 1H), 2.31−2.42 (m, 2H), 3.91−3.98 (m, 2H), 7.05−7.07 (m, 2H), 7.29−7.31 (m, 2H), 7.87 (s, 1H), 7.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 22.4, 29.3, 35.9, 36.6, 42.2, 47.5, 128.8, 132.1, 142.0, 142.7, 142.9, 151.8, 152.0. MS: *m*/*z*: 277, 278 (M + 1). Anal. calcd for $C_{15}H_{20}ClN_3$: C, 64.85; H, 7.26; N, 15.13. Found: C, 64.50; H, 7.21; N, 14.95. $[\alpha]_D^{24} = -14.4$ (*c* 1.0, CH_2Cl_2); 96% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{major} = 14.44$ min, $t_{minor} = 17.33$ min.

*1-[(3S)-3-(4-Chlorophenyl)heptyl]-1H-1,2,4-triazole (***5j***-S).* Colorless oil; yield 74%; $[\alpha]_D^{24} = 16.8$ (*c* 1.0, CH_2Cl_2); 97% ee. The enantiomeric ratio was determined by HPLC on Chiralcel OD-H column (hexane/2-propanol = 90/10, 1 mL/min), $t_{minor} = 13.73$ min, $t_{major} = 17.81$ min. The spectroscopic data were the same as those of **5j**-*R*.

X-ray Diffraction Analysis. Colorless blocks of **5d**-*R* (0.30 mm × 0.20 mm × 0.10 mm) were counted on a quartz fiber with protection oil. Cell dimensions and intensities were measured at 294 K on a Bruker SMART CCD area detector diffractometer with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å); $\theta_{max} = 26.00$; 6810 measured reflections; 1462 independent reflections ($R_{int} = 0.0787$) of which 1251 had $I > 2\sigma(I)$. Data were corrected for Lorentz and polarization effects and for absorption ($T_{min} = 0.9924$; $T_{max} = 0.9774$). The structure was solved by direct methods using SHELXS-2001 (*35*); all other calculations were performed with Bruker SAINT System and Bruker SMART programs (*36*). Full-matrix least-squares refinement based on F^2 using the weight of $1/[\sigma^2(F_o^2) + (0.0849P)^2 + 0.0555P]$ gave final values of $R = 0.0472$, $\omega R = 0.1197$, and GOF(F) = 0.909. Hydrogen atoms were observed and refined with a fixed value of their isotropic displacement parameter.

The crystallographic data have been deposited with Cambridge Crystallographic Data Centre, CCDC No. 691651 for compound **5d**-*R*. Copies of this information can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 IEZ, United Kingdom (Fax: +44-1123-336033; e-mail: deposit@ccdc.ac.uk or http://www.ccdc.cam.ac.uk).

Antifungal Activity Determination. The in vitro fungicidal activities against *F. oxysporum*, *R. solani*, *B. cinereapers*, *G. zeae*, *D. gregaria*, and *C. gossypii* were tested according to the reported method (*37, 38*). The medium was amended with aliquots of each tested compounds solution to provide concentration of 100 mg/L. The tested compounds were dissolved in 0.3 mL of DMF and added aseptically to molten agar after autoclaving, when the agar had cooled to approximately 45−50 °C. The concentration of solvent never exceeded 0.1 mg/L. The mixed medium without sample was used as the blank control. The inocula, 5 mm in diameter, were removed from the margins of actively growing colonies of mycelium, placed in the centers of the above plates. There were three replate plates of compound concentration, and the control plates were sealed with parafilm and incubated at 26 °C in darkness. The diameter of the mycelium was measured for 48 h. The inhibition percent was used to describe the control efficiency of the compounds: inhibition percent (%) = (hyphal diameter in the control − hyphal diameter in the treatment)/hyphal diameter in the control.

RESULTS AND DISCUSSION

Synthesis of Chiral γ-Aryl-1*H*-1,2,4-triazole Derivatives. The use of chiral pesticides has given rise to the research for new and effective methods of obtaining pure chiral compounds. There are two methods used to derive the pure chiral molecules, namely, chiral-controlling synthesis and resolving the enantiomeric mixtures. To get the reactions of Grignard reagents to α,β-unsaturated carbonyl compounds, we use the chiral auxiliary under mild reducing reaction to give enantiomerically pure chiral alcohols (*20*). Furthermore, we used the chiral auxiliary as revulsant to obtain the pure chiral 3*R*- or 3*S*-γ-aryl-1*H*-1,2,4-triazole derivatives. The synthetic route of γ-aryl-1*H*-1,2,4-triazoles **5** is outlined in **Scheme 1**.

Compounds **5** were prepared from *N*-enoylsultams **1**, which were readily obtained by acylation of camphorsultam (as well as their antipode that were readily prepared from camphor on a kg scale) with NaH/acyl chlorides and purified by crystallization using the two methods (*39*). The intermediate **1** was then converted to the chiral amide derivatives **2** by reacting with Grignard reagents RMgX at −78 °C in anhydrous THF under a nitrogen atmosphere. Removing the chiral auxiliary camphorsultam under mild method using $NaBH_4$ (aqueous THF) (*40*), we obtained the various chiral alcohols **3** that were then bromized with CBr_4 in the presence of PPh_3 in CH_2Cl_2. The bromides **4** were then treated with 1*H*-1,2,4-triazole in CH_3CN in the presence of K_2CO_3 at 60−70 °C for 5−7 h to produce the chiral γ-aryl-1*H*-1,2,4-triazoles compounds **5**. In the experimental conditions described herein, the pure 3*R*- and 3*S*-γ-aryl-1*H*-1,2,4-triazole derivatives **5** were obtained conveniently by using the chiral auxiliary (Oppolzer's sultam), with the ee values of the triazoles reaching up to 99%. The ee value and optical rotation properties of the target compounds are shown in **Table 1**. The structures of all newly compounds are elucidated by spectroscopic (^{1}H and ^{13}C NMR) data and elemental analysis. A detailed methodology of obtaining each of compounds **1**−**4** is given in the Materials and Methods.

As indicated in **Table 1**, the target molecules have moderate to high ee values. The ee values of compounds **5a**-*R*, **5a**-*S*, **5d**-*R*, **5e**-*S*, **5j**-*R*, and **5j**-*S* are more than 95%. The difference of substitutes and configuration leads to the different ee values. The configurations of compounds **5** were assigned through the absolute configuration of compounds **2** and **3** (*20*).

Crystal Structure Analysis. The crystal structure of target molecule **5d**-*R* is established using X-ray crystallographic diffraction analysis as shown in **Figures 2** and **3**. In compound **5d**-*R*, the bond lengths N(1)−C(1) [1.311(5) Å] and N(3)−C(2) [1.307(5) Å] are close to the C=N double bond distance (1.34 Å). The bond length C(9)−O(1) is 1.377(3) Å. The benzene ring [C(6), C(7), C(8), C(9), C(10), C(11)] and the adjacent carbon atom C(5) are fairly planar, and the deviation from the least-squares plane through the ring atoms is less than 0.004 Å. The dihedral angle between the plane of benzene and the plane of the triazole group is 89.51°, and the adjacent carbon atom C(3) linked to the later is all fairly planar. The deviation from the least-squares plane through the ring atoms is less than 0.006 Å. As shown in the packing diagram of the compound **5d**-*R* (**Figure 3**), there exist no classic hydrogen bonds. However, the weak interactions occurring between intermol-

ecules of C−H···N and molecules are linked via an intermolecular C−H−π interactions of C(14)−H(14c) to the benzene ring.

Antifungal Activity. The antifungal activities of compounds **5** were evaluated using in vitro agar diffusion and broth dilution assay, the results of which are presented in **Table 2**. Most of the compounds showed activity in the initial screening against fungal cultures when tested at 100 μg/mL concentration using agar diffusion assay. Compounds **5c**-*R*, **5e**-*R*, **5f**-*R*, **5g**-*S*, **5h**-*R*, **5i**-*R*, **5i**-*S*, and **5j**-*R* inhibited the growth of the drug-resistant species of *F. oxysporum*, *R. solani*, *B. cinereapers*, *G. zeae*, *D. gregaria*, and *C. gossypii*. They showed significant activity against all fungal cultures.

In **Table 2**, the structure−activity relationships clearly suggest that *n*-butyl substitution on the γ-position of the triazole ring in compounds **5h**−**j** is responsible for the broad spectrum and high antifungal activity. The presence of the groups like 4-Cl (**5c**-*R*, **5j**-*R*, and **5j**-*S*), 4-OMe (**5g**-*S*), and 4-F (**5f**-*R*, **5i**-*R*, and **5i**-*S*) substitution on the phenyl ring also plays a significant role in imparting antifungal activity to the compounds.

Compounds **5a**−**j** were prepared as single enantiomers and assayed. To sum it all, the *R*-forms were found to be more active than the *S*-forms (**5c**-*R*, **5e**-*R*, **5f**-*R*, **5h**-*R*, **5i**-*R*, and **5j**-*R*), while the compound **5g**-*S* was more active than the compound **5g**-*R*.

Comparison with the Reference Compound Bayleton. Bayleton, a broad spectra fungicide, was first introduced as a triazole fungicide in the year 1976. We used this compound as a reference to further study the activity of the potential compounds **5i**-*R* and **5i**-*S* at the lower concentration of 50 μg/mL. **Tables 3** and **4** show the in vitro activity of compounds **5i**-*R* and **5i**-*S* against *F. oxysporum*, *R. solani*, *B. cinereapers*, *G. zeae*, *D. gregaria*, and *C. gossypii* species as compared to those of Bayleton at the same level. The compound **5i**-*R* had a comparably high inhibitory activity and broad spectra of activity as compared to Bayleton against all of the fungal pathogens tested, especially to the *G. zeae* and *D. gregaria*, which reached the inhibition rate of 89 and 100%, respectively. The values of EC_{50} (50% effective concentration) of compounds **5i**-*R* and **5i**-*S* are shown in **Table 4**.

In conclusion, a novel series of antifungal agents chiral γ-aryl-1*H*-1,2,4-triazole derivatives have been designed and synthesized conveniently by using the chiral auxiliary as a controlling reagent. All of the compounds exhibit moderate to high ee values reaching up to 99%, and the preliminary bioassay results demonstrated that most of the compounds take on a significantly wide spectrum activity against *F. oxysporum*, *R. solani*, *B. cinereapers*, *G. zeae*, *D. gregaria*, and *C. gossypii* species. The pure optical enantiomer **5i**-*R* showed a better activity against *G. zeae* and *D. gregaria* than the commercial compound Bayleton, which may be the most potential active compound for further structure optimization.

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