Synthesis of 2,3-Diaryl-3,4-dihydro-2*H*-1,3-benzoxazines and Their Fungicidal Activities

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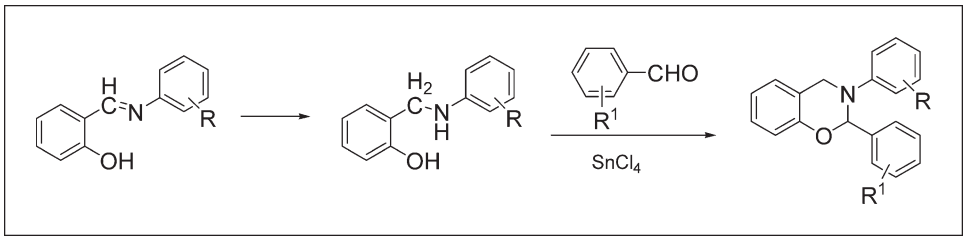

A series of novel 2,3-diaryl-3,4-dihydro-*2H*-1,3-benzoxazines have been prepared in high yields from *o*-arylaminomethylphenols and aromatic aldehydes in the presence of $SnCl_4$ for the first time, and their fungicidal activities were investigated too. Some of the products showed good fungicidal activities against *Rhizoctonia solani* justified by 100% activity of compound **1b**.

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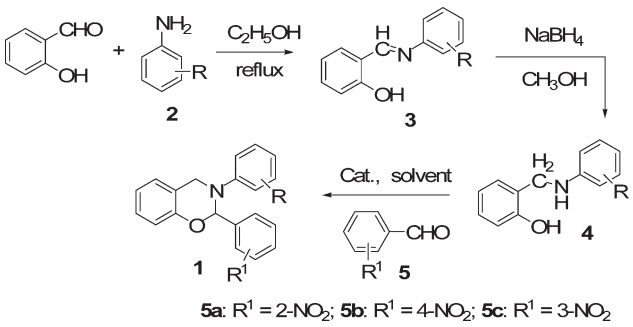
INTRODUCTION

As 3,4-dihydro-2*H*-1,3-benzoxazines and 3,4-dihydro-2*H*-1,3-oxazine containing compounds have been reported to show different antimicrobial properties [1], such as bactericidal, fungicidal, and many pharmacological features [2] such as antitumour, antituberculosis, and anthelmintic activity, these types of compounds have been an important subject of researches. In addition, *N*-substituted 3,4-dihydro-2*H*-1,3-benzoxazines are potential intermediates for the preparation of phenol-formaldehyde resins [3]. Hence, the synthesis of these compounds including the synthesis of benzoxazine monomers containing special functional group has attracted great interest. Several methods have been reported for the preparation of these compounds in the literature. For example, an important method was developed by Burke et al. [4], using Mannich-type condensation of phenols with primary amines and two equivalents of formaldehyde. Condensations of *o*-aminomethylphenol with aldehydes or ketones provided another route [5]. Reactions of primary amines with oxygen-containing dihalocompounds established a way to prepare 3,4-dissymmetric-substituted 3,4-dihydro-1,3-benzoxazines [6]. Recently, rhodium-catalyzed reactions of 2-(alkenyloxy)benzylamines have been developed as a new way to generate 3,4-dihydro-1,3-benzoxazines, which involves an allylic cleavage followed by regioselective carbonylation at the internal carbon atom [7]. However, some drawbacks existed in previous methods. Hence, both the preparation of novel 3,4-dihydro-1,3-benzoxazines and the development of efficient method are still of great importance. On the other hand, the reported biological studies of dihydro-1,3-benzoxazines were mainly focused on the pharmacological activities. To the best of our knowledge, few papers about the pesticidal activities of dihydro-2*H*-1,3-benzoxazines and the preparation of 2,3-diaryl-3,4-dihydro-2*H*-1,3-benzoxazines have been reported. Hence, herein, we present our results of the synthesis of 2,3-diaryl-3,4-dihydro-2*H*-1,3-benzoxazines mediated by $SnCl_4$ (Scheme 1) and the preliminary fungicidal activities of the products.

RESULTS AND DISCUSSION

The intermediate Schiff bases **3** were smoothly prepared in 84 to 99% yields (Table 1) by condensation reactions of substituted anilines **2** with salicylaldehyde, and followed by reduction with $NaBH_4$ affording *o*-arylaminomethylphenols **4** in 90 to 94% yields (Table 1) [8,9]. It was found that only *E* isomer of Schiff base **3** was formed [9], possibly due to the stability and a hydrogen bond between the hydroxyl group and the nitrogen atom [9,10]. Then, reaction of *o*-aminomethyl phenol **4c** with 3-nitrobenzaldehyde **5c** in the presence of *p*-toluenesulfonic acid (TsOH) [**2g**,11] was performed under reflux by removing the water of condensation

Scheme 1. Synthesis of 2,3-diaryl-3,4-dihydro-2*H*-1,3-benzoxazines **1**.



with chloroform azeotropically to prepare 2,3-diaryl-3,4-dihydro-2*H*-1,3-benzoxazine **1a**, the reaction gave the desired product in only 11% yield along with an unknown white solid (Table 2, entry 1). We next attempted a mixed solvent of chloroform and cyclohexane, (v:v = 1:7) taking into account the higher azeotropic ability of cyclohexane, the yield raised to 18% (entry 2), but still far away from satisfaction. Here, it should be noted that the addition of chloroform was to increase the solubility of reactants. In literature, Lewis acid $SnCl_4$ was reported as an effective catalyst for many reactions, such as acetalization and ketalization of aldehydes or ketones [12]. Therefore, we tried $SnCl_4$ (20 mol %) as catalyst, to our delight, it turned out that the reaction of **4c** with **5c** in chloroform/cyclohexane (v:v = 1:7) gave product **1a** in 95% yield at 85°C (entry 3). To the best of our knowledge, this is the first time to use $SnCl_4$ as catalyst for the zaz-acetalization of aromatic aldehyde with *o*-aminomethylphenol to prepare dihydro-1,3-benzoxazine. But, the yield decreased when the amount of the catalyst was increased to 25 mol % (entry 4). Thus, we employed 20 mol % of $SnCl_4$ for the synthesis of compounds **1b–1o**. Generally, under these conditions, **1b–1o** were prepared in 60 to 80% yields (entries 3–18). Compounds possessing an electron-releasing group on the phenyl group bond to the nitrogen atom gave higher yields than those with an electro-withdrawing group. Electron-releasing group increases the electron density of the nitrogen and hence increases its nucleophilicity. Moreover, it was observed that, for compounds containing a methyl group on the benzene ring connected with the nitrogen atom, the yield mainly depended on the position of the methyl group in the order of *para* > *meto* > *ortho* regardless of the nature of the aryl group at position-2 of the oxazine ring. The last two cases may be attributed to the steric hindrace.

The structures of all the synthesized compounds were established on the basis of their spectroscopic data and elemental analysis. For compound **1b**, strong absorptions at 1530 and 1337 cm^{-1} are attributed to the antisymmetrical and symmetrical stretch vibration absorption of the NO_2 group, and 1585 and 1610 cm^{-1} for νC=C bond. δ = 6.85 observed in ^{1}H-NMR corresponds to OCHN proton of benzoxazine ring. The downfield shift of OCHN proton is due to the strong electron negative of nitrogen and oxygen atoms. Particularly, the proton of NCH_2 group absorbs as two doublets at 4.00 and 4.19 instead of a singlet. These data strongly suggested the formation of benzoxazine ring. In addition, the spectroscopic data-based structure was further confirmed by X-ray crystallographic analysis of **1b** (Fig. 1) [13]. It can be seen clearly from the structure, in solid state, the conformation of oxazine ring is a half-chair form with two trans-axial orientation of both the *N*-aryl and 2-aryl group. It apparently indicated that the nitrogen atom adopted sp^3 hybrid orbital.

According to SOP procedure [14], fungicidal activities of the prepared compound **1a–1o** against *Gibberella zeae, Phytophythora capsici, Alternaria alternate*, *Botrytis cinerea*, and *Sclerotonia sclerotiorum* were evaluated using the mycelium growth rate test in concentration of 25 mg/L, which was expressed as inhibition rate (%), and their activities against *Rhizoctonia solani* using the leaf-disc culture in concentration of 500 mg/L, which was expressed as control efficacy (%). The results are summarized in Table 3. In principle, it can be seen that most of the compounds showed moderate to good activity. For the tested compounds, the activity against *Rhizoctonia solani* was the best as shown by compound **1b** (100%) and **1e, 1g, and 1n** (80% for three compounds). Moreover, compounds possessing an electron-releasing group on the phenyl group bond to the nitrogen atom showed higher activities against *Rhizoctonia solani* than those with an electro-withdrawing group. For other fungus, there was not apparent structure-activity relationship. The insecticidal activities of the compounds **1** are in progress.

EXPERIMENTAL

All solvents were dried by standard procedure. Aromatic aldehydes and substituted anilines were commercially

Table 1

The results of the preparation of Schiff base **3** and *o*-aminomethylphenol **4**.

Entry	R	Product 3	Yield[a] (%)	Product 4	Yield[b] (%)
1	2-CH_3	**3a**	90	**4a**	91
2	3-CH_3	**3b**	84	**4b**	94
3	4-CH_3	**3c**	98	**4c**	94
4	4-Cl	**3d**	98	**4d**	90
5	4-OCH_3	**3e**	93	**4e**	92
6	H	**3f**	91	**4f**	91

[a] Isolated yield for reaction carried out in refluxing ethanol for 3 h.
[b] Isolated yield for reaction carried out in methanol at 0°C for 40 min.

Table 2

The results of the preparation of compound **1**.

Entry	R	R^1	Conditions[a]	Product	Yield[b] (%)
1	4-CH_3	3-NO_2	TsOH (20 mol %), $CHCl_3$, reflux, 5 h	**1a**	11[c]
2	4-CH_3	3-NO_2	TsOH (20 mol %), reflux, 5 h, $CHCl_3/C_6H_{12}$	**1a**	18
3	4-CH_3	3-NO_2	$SnCl_4$(20 mol %), 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1a**	95
4	4-CH_3	3-NO_2	$SnCl_4$ (25 mol %), 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1a**	85
5	4-CH_3	2-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1b**	80
6	4-CH_3	4-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1c**	67
7	3-CH_3	2-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1d**	69
8	3-CH_3	3-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1e**	68
9	3-CH_3	4-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1f**	65
10	2-CH_3	2-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1g**	63
11	2-CH_3	3-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1h**	65
12	2-CH_3	4-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1i**	64
13	4-Cl	2-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1j**	69
14	4-Cl	4-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1k**	60
15	H	2-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1l**	66
16	H	3-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1m**	61
17	4-CH_3O	2-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1n**	73
18	4-CH_3O	3-NO_2	$SnCl_4$, 85°C, 5 h, $CHCl_3/C_6H_{12}$	**1o**	70

[a] The mole ratio of *n* (aromatic aldehyde **5**): *n* (aminomethyl phenol **4**) = 1.3:1 for all reactions. The amount of $SnCl_4$: 20 mol % based on aminomethyl phenol except for the cases marked in the table. C_6H_{12}: cyclohexane; $CHCl_3$:C_6H_{12} = 1:7 (v:v).
[b] Isolated yield.
[c] An unknown white solid also formed.

available. Infrared spectra were recorded on a PE-2000 FT-IR. ^{1}H and ^{13}C-NMR spectra were recorded on Bruker Avance-500 MHz spectrometer. Chemical shifts (δ) are given in ppm relative to Me_4Si (0, ^{1}H) or $CDCl_3$ (77.0, ^{13}C). Mass spectra were obtained with Thermo Finnigan LCQ Advantage spectrometer. Elemental analysis was measured on PE 2400 II CHNS instrument. Melting points were determined on a WRS-1B digital melting point instrument and without correction. Thin-layer chromatography (TLC) was run on precoated silica gel plates (Merck 60F_{254}). Column chromatography was carried out using flash silica gel. X-ray crystallographic analysis was performed on a Bruker Smart CCD diffractometer equipped with a graphite monochromator Mo Kα radiation (λ = 0.71073 Å).

Schiff bases **3a–f** and corresponding *o*-arylaminomethyl phenols **4a–f** were prepared according to the method described in references [8,9].

General procedure for the synthesis of 2,3-diaryl-3,4-dihydro-2*H*-1,3-benzoxazines 1a-1o. Under nitrogen, into a 250-mL three-necked flask equipped with a Dean-stark, 2-((*p*-toluidino)methyl)phenol **4c** (1.07 g, 5 mmol), 3-nitrobenzaldehyde (0.98 g, 6.5 mmol), mixed solvent of chloroform and cyclohexane (150 mL, v:v = 1:7), and $SnCl_4$ (0.26 g, 20 mol %) were added and mixed with stirring. The solution was heated at 85°C for 5 h (checked by TLC), and the water of condensation was removed by azeotropic distillation. Then, triethyl amine was added to make solution at pH = 8, followed by addition of ethyl acetate (100 mL), and washed sequentially with water (2 × 100 mL) and saturated brine (2 × 100 mL). The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The obtained yellow oil was purified by flash column chromatography (silica gel, PE-EtOAc) affording the product **1a** (1.64 g, 95% yield) as a yellow solid.

2-(3-Nitrophenyl)-3-*p*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1a). Yield 95%, m.p.: 123.6–125.5°C; IR (KBr): 3093, 3070, 3022, 2978, 2857, 1611, 1583, 1528, 1513, 1490, 1457, 1380, 1346, 1272, 1265, 1227, 1197, 1149, 1127, 1108, 1083, 1033, 995, 956, 941, 923, 893, 821, 811, 805, 752, 734, 711, 694, 670, 594 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.27 (s, 3H, CH_3), 4.25 (d, *J* = 17.0 Hz, 1H, CH_2), 4.35 (d, *J* = 17.0 Hz, 1H, CH_2), 6.56 (s, 1H, CH), 6.86 (d, *J* = 8.0 Hz, 2H), 7.02–7.03 (m, 1H), 7.07–7.12 (m, 4H), 7.16 (d, *J* = 2.5 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 8.15–8.17 (m, 1H), 8.45 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 20.68, 47.20, 87.61, 117.09, 120.14, 121.01 (2C), 121.16, 122.29, 123.23, 126.67, 128.37, 129.69, 129.91 (2C), 132.58, 133.09, 141.64, 146.95, 148.70, 152.39; MS (EI, 70 ev) *m/z* (%): 346 (30) [M^+], 240 (100), 223 (6), 193 (8), 165 (4), 118 (14), 107 (4), 91 (25), 77 (9), 65 (9), 51 (4); Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 72.53; H 5.22; N 8.06.

2-(2-Nitrophenyl)-3-*p*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1b). Yield 80%, m.p.:152.6–153.0°C; IR (KBr): 3083, 3021, 2972, 2920, 1610, 1585, 1530, 1513, 1486, 1456, 1437, 1386, 1363, 1337, 1292, 1276, 1268, 1224, 1198, 1144, 1109, 1034, 1024, 1015, 978, 961, 935, 852, 839, 820, 782, 757, 736, 714, 687, 679, 632, 589 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.25 (s, 3H, CH_3), 4.00 (d, *J* = 17.0 Hz, 1H, CH_2), 4.19 (d, *J* = 17.0 Hz, 1H, CH_2), 6.85 (s, 1H, CH), 6.86–6.88 (m, 1H), 7.00–7.06 (m, 6H), 7.17–7.20 (m, 1H), 7.44–7.47 (m, 2H), 7.61–7.63 (m, 1H), 7.72–7.74 (m, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 20.74, 47.12, 85.52, 116.72, 120.45, 120.86 (2C), 121.13, 124.45, 126.72, 128.41, 128.76, 129.21, 129.80 (2C), 131.84, 132.76, 132.99, 146.74, 149.08, 152.60; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 73.11; H 5.26; N 8.05.

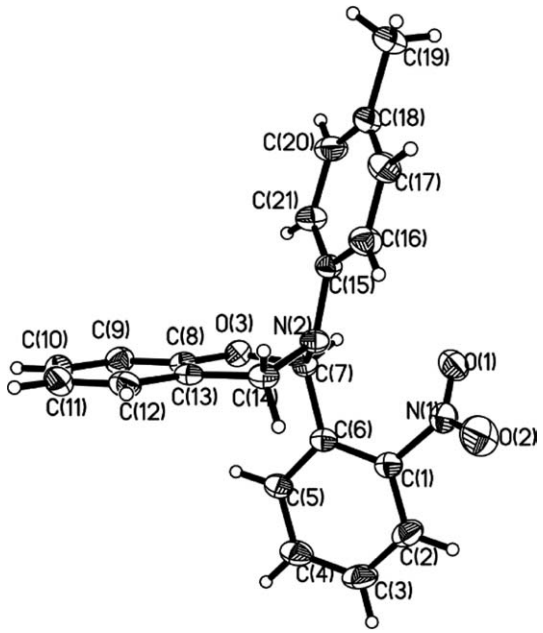


Figure 1. ORTEP diagram of compound **1b**.

2-(4-Nitrophenyl)-3-*p*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1c). Yield 67%, m.p.: 93.7–96.9°C; IR (KBr): 2920, 2859, 1614, 1583, 1516, 1490, 1455, 1442, 1386, 1343, 1318, 13002, 1224, 1205, 1144, 1109, 1033, 1014, 976, 960, 940, 905, 854, 829, 812, 760, 739, 712, 696, 589 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.27 (s, 3H, CH_3), 4.22 (d, J = 17.0 Hz, 1H, CH_2), 4.34 (d, J = 16.5 Hz, 1H, CH_2), 6.57 (s, 1H, CH), 6.86–6.88 (m, 2H), 6.99 (d, J = 3.5 Hz, 1H), 7.06–7.10 (m, 4H), 7.16–7.19 (m, 1H), 7.74 (d, J = 8.5 Hz, 2H), 8.18–8.21 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 20.64, 47.13, 87.72, 116.94, 120.10, 120.73 (3C), 121.14, 123.83, 123.99, 126.67, 127.92, 128.29, 129.87 (2C), 132.44, 146.41, 145.85, 147.69, 152.38; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 72.54; H 5.28; N 8.12.

2-(2-Nitrophenyl)-3-*m*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1d). Yield 69%, m.p.: 138.1–139.0°C; IR (KBr): 3072, 2947, 2906, 2862, 1606, 1586, 1535, 1489, 1456, 1445, 1378, 1340, 1301, 1273, 1236, 1216, 1199, 1169, 1140, 1109, 1036, 983, 958, 937, 852, 837, 782, 772, 756, 737, 690, 634, 597 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.30 (s, 3H, CH_3), 4.01 (d, J = 17.0 Hz, 1H, CH_2), 4.23 (dd, J = 1.0 Hz, J = 1.0 Hz, 1H, CH_2), 6.80(d, J = 7.5 Hz, 1H), 6.85–6.87 (m, 2H), 6.93–6.95 (m, 1H), 6.98 (s, 1H, CH), 7.01 (d, J = 8.0 Hz, 1H), 7.08 (s, 1H), 7.11 (t, J = 8.0 Hz, 1H), 7.17–7.20 (m, 1H), 7.43–7.48 (m, 2H), 7.61–7.62 (m, 1H), 7.73–7.74 (m, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 21.72, 46.79, 85.03, 116.76, 117.27, 120.41, 121.05 (2C), 121.13, 123.91, 124.47, 126.66, 128.41, 128.78, 129.02, 129.22, 131.83, 132.99, 139.02, 149.10, 152.44; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 73.12; H 5.28; N 8.06.

2-(3-Nitrophenyl)-3-*m*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1e). Yield 68%, m.p.: 101.3–102.0°C; IR (KBr): 3092, 3025, 2979, 2918, 1602, 1585, 1529, 1488, 1475, 1380, 1348, 1314, 1271, 1238, 1219, 1181, 1123, 1113, 1087, 1046, 1032, 994, 958, 970, 942, 899, 891, 806, 776, 753, 735, 696, 688, 671, 599 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.32 (s, 3H, CH_3), 4.26 (d, J = 17.0 Hz, 1H, CH_2), 4.37 (d, J = 17.0 Hz, 1H, CH_2), 6.63 (s, 1H, CH), 6.82–6.89 (m, 3H), 7.00–7.04 (m, 3H), 7.15–7.19 (m, 2H), 7.51 (t, J = 8.0 Hz, 1H), 7.89–7.91 (m, 1H), 8.15–8.17 (m, 1H), 8.44 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 21.65, 46.56, 86.98, 117.11, 117.24, 120.05, 121.07, 121.13, 122.20, 123.22, 123.54, 126.60, 128.35, 129.17, 129.72, 133.04, 139.24, 141.60, 148.64, 149.36, 152.15; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 72.53; H 5.20; N 8.05.

2-(4-Nitrophenyl)-3-*m*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1f). Yield 65%, m.p.: 126.2–126.9°C; IR (KBr): 3042, 2976, 2876, 1607, 1584, 1554, 1541, 1512, 1489, 1456, 1378, 1350, 1306, 1239, 1221, 1189, 1169, 1128, 1110, 1038, 981, 956, 857, 826, 783, 767, 752, 739, 694, 609 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.32 (s, 3H, CH_3), 4.24 (d, J = 16.0 Hz, 1H, CH_2), 4.38 (d, J = 7.0 Hz, 1H, CH_2), 6.65 (s, 1H, CH), 6.83 (t, J = 7.5 Hz, 1H), 6.85 (t, J = 5.0 Hz, 2H), 7.00 (dd, J

Table 3

Fungicidal activities of compounds **1a–1o**.

Compound	*Gibberella zeae* (%)	*Phytophythora capsici* (%)	*Alternaria alternate* (%)	*Botrytis cinerea* (%)	*Rhizoctonia solani* (%)	*Sclerotonia sclerotiorum* (%)
1a	10.3	37.4	17.5	13.6	50.0	0
1b	30.9	28.0	10.5	19.0	100	59.8
1c	30.9	28.0	0	13.6	0	0
1d	39.2	33.6	14.0	6.8	50.5	56.1
1e	30.9	9.3	35.1	27.2	80.0	0
1f	30.9	37.4	10.5	20.4	0	0
1g	20.6	28.0	14.0	33.3	80.0	0
1h	20.6	28.0	10.5	33.3	0	0
1i	20.6	28.0	7.0	27.2	60.0	0
1j	30.9	31.8	42.1	47.6	0	75
1k	41.2	37.4	38.6	47.6	10.0	28.0
1l	30.9	31.8	17.5	23.1	50.0	0
1m	24.7	22.4	3.5	13.6	70.0	0
1n	51.5	37.4	45.6	27.2	80.0	56.1
1o	10.3	18.6	0	13.6	0	0

= 7.0 Hz, *J* = 3.5 Hz, 3H), 7.16–7.20 (m, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 8.19 (d, *J* = 8.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 21.69, 46.66, 87.22, 117.07, 117.12, 120.16, 120.92, 121.21, 123.53(2C), 123.91, 126.69, 127.95(2C), 128.36, 129.25, 139.31, 146.51, 147.81, 149.36, 152.32; MS (ESI): 347[M+H]$^+$. Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 73.60; H 5.21; N 8.13.

2-(2-Nitrophenyl)-3-*o*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1g). Yield 63%, m.p.: 164.3–165.3°C; IR (KBr): 3079, 3025, 2948, 2913, 1608, 1597, 1588, 1527, 1458, 1439, 1365, 1338, 1300, 1274, 1228, 1207, 1187, 1142, 1118, 1057, 1035, 1021, 977, 955, 937, 855, 841, 827, 780, 760, 737, 725, 714, 684, 663, 634, 592 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.20 (s, 3H, CH_3), 3.93 (s, 2H, CH_2), 6.76 (d, *J* = 12.0 Hz, 1H), 6.83–6.86 (m, 1H), 6.98 (s, 1H, CH), 6.99–7.01 (dd, *J* = 7.4 Hz, *J* = 0.9 Hz, 1H), 7.03 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 7.0 Hz, 1H), 7.20–7.23 (m, 1H), 7.43–7.51 (m, 3H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.78 (dd, *J* = 1.5 Hz, *J* = 1.0 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 17.93, 47.84, 85.79, 116.61, 119.57, 121.08, 122.95, 124.92 (2C), 126.64, 127.06, 128.47, 128.77, 129.13, 131.19, 132.11, 133.17, 133.37, 148.11, 148.79, 152.44; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 72.51; H 5.21; N 8.05.

2-(3-Nitrophenyl)-3-*o*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1h). Yield 65%, m.p.: 85.0–86.1°C; IR (KBr): 3023, 2933, 2885, 1598, 1585, 1533, 1490, 1456, 1434, 1386, 1380, 1349, 1336, 1227, 1215, 1188, 1149, 1082, 1033, 986, 959, 893, 807, 764, 755, 742 724, 695, 673, 588 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.51 (s, 3H, CH_3), 4.14 (d, *J* = 17.0 Hz, 1H, CH_2), 4.25 (d, *J* = 17.0 Hz, 1H, CH_2), 6.34 (s, 1H, CH), 6.86–6.92 (m, 2H), 7.05–7.13 (m, 3H), 7.20–7.25 (m, 2H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 2.5 Hz, 1H), 8.16–8.18 (m, 1H), 8.54–8.55 (m, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 18.59, 47.37, 87.92, 117.08, 119.86, 121.15, 122.35, 123.10, 123.31, 125.03, 126.69, 126.86, 128.23, 129.57, 131.07, 133.13, 133.17, 141.43, 148.11, 148.52, 152.28; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09%. Found: C 73.12; H 5.28; N 8.06.

2-(4-Nitrophenyl)-3-*o*-tolyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1i). Yield 64%, m.p.: 128.5–129.8°C; IR (KBr): 3074, 2955, 2886, 1607, 1584, 1520, 1486, 1456, 1380, 1345, 1333, 1228, 1214, 1183, 1140, 1106, 1033, 1019, 1011, 975, 953, 932, 858, 837, 763, 752, 742, 723, 709, 601 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.50 (s, 3H, CH_3), 4.12 (d, *J* = 16.5 Hz, 1H, CH_2), 4.23 (d, *J* = 17.0 Hz, 1H, CH_2), 6.35 (s, 1H, CH), 6.86–6.92 (m, 2H), 7.05–7.11 (m, 3H), 7.22–7.26 (m, 2H), 7.36–7.38 (m, 1H), 7.84 (d, *J* = 8.5 Hz, 2H), 8.22–8.23 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 18.59, 47.40, 88.16, 116.97, 119.89, 121.17, 123.19, 123.75, 124.25, 125.02, 126.73, 126.88, 128.03, 128.21, 130.44, 131.08, 133.04, 146.32, 147.61, 148.18, 152.35; MS (ESI): 347[M+H]$^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C 72.51; H 5.20; N 8.04.

3-(4-Chlorophenyl)-2-(2-nitrophenyl)-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1j). Yield 69%, m.p.: 140.7–141.3°C; IR (KBr): 3035, 2936, 2875, 1609, 1592, 1522, 1494, 1457, 1384, 1361, 1342, 1304, 1276, 1224, 1203, 1113, 1098, 1034, 1020, 1008, 980, 949, 936, 855, 826, 782 750, 740, 727, 645, 596 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 3.99 (d, *J* = 17.0 Hz, 1H, CH_2), 4.22 (d, *J* = 17.0 Hz, 1H, CH_2), 6.85 (s, 1H, CH), 6.87–6.91 (m, 1H), 7.00 (d, *J* = 9.5 Hz, 2H), 7.06–7.09 (m, 2H), 7.17–7.22 (m, 3H), 7.44–7.49 (m, 2H), 7.59–7.62 (m, 1H), 7.73–7.77 (m, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 46.95, 85.09, 116.67, 119.81, 121.28, 121.98 (2C), 124.49, 126.60, 128.25, 128.57, 128.61, 129.14 (2C), 129.33, 131.94, 132.40, 147.54, 148.77, 152.28; MS (ESI): 367 [M+H]$^+$; Anal. Calcd. for $C_{20}H_{15}ClN_2O_3$: C 65.49; H 4.12; N 7.64. Found: C 65.75; H 4.10; N 7.68.

3-(4-Chlorophenyl)-2-(4-nitrophenyl)-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1k). Yield 60%, m.p.: 135.9–137.6°C; IR (KBr): 3075, 3057, 2938, 2973, 2891, 2851, 1605, 1593, 1583, 1516, 1496, 1487, 1455, 1373, 1348, 1331, 1288, 1224, 1199, 1182, 1131, 1112, 1034, 1005, 963, 930, 902, 855, 830, 819, 800, 753, 743, 724, 711, 642, 624, 602, 559 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 4.24 (d, *J* = 17.0 Hz, 1H, CH_2), 4.34 (d, *J* = 1 7.0 Hz, 1H, CH_2), 6.56 (s, 1H, CH), 6.89–6.94 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.11–7.12 (m, 2H), 7.17–7.19 (m, 1H), 7.20–7.24 (m, 2H), 7.72–7.74 (m, 2H), 8.19–8.21 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 47.24, 87.23, 117.02, 119.61, 121.39, 121.90 (3C), 123.90 (2C), 126.66, 127.84, 127.90 (2C), 128.53, 129.29 (2C), 145.83, 147.78, 152.12; MS (EI, 70 ev) *m*/*z* (%): 366 (35) [M$^+$], 260 (100), 213 (17), 178 (4%), 138 (10), 111 (12), 78 (7), 51 (5); Anal. Calcd. for $C_{20}H_{15}ClN_2O_3$: C 65.49; H 4.12; N 7.64. Found: C 65.15; H 4.08; N 7.60.

2-(2-Nitrophenyl)-3-phenyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1l). Yield 66%, m.p.: 130.9–131.7°C; IR (KBr): 3023, 2948, 2860, 1598, 1585, 1535, 1496, 1486, 1455, 1396, 1365, 1273, 1223, 1136, 1110, 1036, 981, 957, 853, 783, 756, 735, 717, 694, 591 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 4.04 (d, *J* = 17.0 Hz, 1H, CH_2), 4.26 (d, *J* = 17.0 Hz, 1H, CH_2), 6.89 (s, 1H, CH), 6.92–6.94 (m, 1H), 6.96–7.03 (m, 2H), 7.11 (s, 1H), 7.16–7.23 (m, 3H), 7.25–7.28 (m, 2H), 7.46–7.49 (m, 2H), 7.63–7.65 (m, 1H), 7.75-–7.77 (m, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 46.78, 85.24, 116.75, 120.36, 120.55 (3C), 121.20, 123.12, 124.50, 126.69, 128.47, 128.79, 129.26 (3C), 131.88, 132.87, 149.08, 152.50; MS(EI, 70 ev) *m*/*z* (%) = 332 (29) [M$^+$], 315 (22), 284 (4), 226 (10), 209 (72), 196 (12), 181 (12), 179 (28), 151 (19), 152 (36), 134 (7), 120 (6), 104 (20), 92 (23), 77 (100), 65 (9), 51 (41); Anal. Calcd. for $C_{20}H_{16}N_2O_3$: C 72.28; H 4.85; N 8.43. Found: C 71.95; H 4.82; N 8.39.

2-(3-Nitrophenyl)-3-phenyl-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1m). Yield 61%, m.p.: 90.3–91.8°C; IR (KBr): 3030, 2962, 2875, 1605, 1502, 1488, 1456, 1398, 1364, 1252, 1227, 1138, 1127, 1085, 994, 957, 893, 783, 757, 735, 713, 694, 592 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 4.04(d, *J* = 17.0 Hz, 1H, CH_2), 4.26 (d, *J* = 17.0 Hz, 1H, CH_2), 6.62 (s, 1H, CH), 6.82–6.92 (m, 3H), 7.02–7.06 (m, 3H), 7.16–7.20 (m, 2H), 7.25–7.28 (m, 1H), 7.51–7.55 (m, 2H), 7.66–7.76 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 47.02, 87.23, 116.90, 120.45, 120.62 (3C), 121.41, 123.22, 125.00, 126.73, 128.51, 129.02, 129.28 (3C), 132.11, 132.90, 149.09, 152.78; MS (ESI): 333 [M+H]$^+$; Anal. Calcd. for $C_{20}H_{16}N_2O_3$: C 72.28; H 4.85; N 8.43. Found: C 72.65; H 4.81; N 8.38.

3-(4-Methoxyphenyl)-2-(2-nitrophenyl)-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1n). Yield 73%, m.p.: 165.-166.9°C; IR (KBr): 3076, 2968, 1607, 1579, 1531, 1509, 1488, 1456, 1388, 1364, 1299, 1270, 1242, 1225, 1199, 1145, 1108, 1034, 1022, 975, 960, 854, 830, 783, 758, 737, 685, 631, 589 cm^{-1}; ^{1}H-

NMR ($CDCl_3$, 500 MHz): δ 3.75 (s, 3H, OCH_3), 4.01 (d, J = 17.0 Hz, 1H, CH_2), 4.17(d, J = 17.0 Hz, 1H, CH_2), 6.77–6.79 (m, 2H), 6.87–6.92 (m, 2H), 6.94 (s, 1H, CH), 7.04 (d, J = 8.0 Hz, 1H), 7.09–7.11 (m, 2H), 7.21–7.25 (m, 1H), 7.46–7.48 (m, 2H), 7.64–7.66 (m, 1H), 7.75–7.76 (m, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 47.48, 55.29, 85.96, 114.17 (2C), 116.59, 120.41, 121.06, 123.18 (2C), 124.28, 126.64, 128.27, 128.59, 129.06, 131.75, 132.77, 142.48, 148.95, 152.63, 155.92; MS (ESI): 363 $[M+H]^+$; Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 69.60; H 5.01; N 7.73. Found: C 69.31; H 4.98; N 7.69.

3-(4-Methoxyphenyl)-2-(3-nitrophenyl)-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (1o). Yield 70%, m.p.: 103.2–106.1°C; IR (KBr): 3070, 3093, 2950, 2832, 1610, 1582, 1528, 1512, 1488, 1456, 1345, 1252, 1227, 1197, 1179, 1127, 1085, 1038, 994, 957, 893, 826, 783, 757, 735, 712, 694, 670 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 3.77 (s, 3H, OCH_3), 4.26 (d, J = 17.0 Hz, 1H, CH_2), 4.34 (d, J = 17.0 Hz, 1H, CH_2), 6.48 (s, 1H, CH), 6.81–6.83 (m, 2H), 6.90–6.91 (m, 2H), 7.05 (d, J = 8.0 Hz, 1H), 7.16–7.18 (m, 2H), 7.20–7.23 (m, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 8.17–8.1 9(m, 1H), 8.49 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 47.99, 55.36, 88.17, 114.31(2C), 116.96, 120.10, 121.10, 122.22, 123.12, 123.34(2C), 126.60, 128.25, 129.54, 133.07, 141.41, 142.61, 148.50, 152.44, 155.77; MS(EI, 70 ev) m/z (%) = 362 (72) $[M^+]$, 345(17), 256(100), 239(38), 227(7), 209(11), 196(19), 183(8), 168(48), 152(10), 1D40(19), 135(30), 122(51), 106(25), 92(20), 77(41), 64(19); Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C 69.60; H 5.01; N 7.73. Found: C 69.85; H 5.05; N 7.69.

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