

Article

Design, Synthesis and Antifungal/Insecticidal Evaluation of Novel Cinnamide Derivatives

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Abstract: Twenty novel cinnamamide derivatives were designed and synthesized using as lead compound pyrimorph, whose morpholine moiety was replaced by β -phenylethylamine. All the compounds were characterized by their spectroscopic data. The fungicidal and insecticidal activities were also evaluated. The preliminary results showed that all the title compounds had certain fungicidal activities against seven plant pathogens at a concentration of 50 $\mu\text{g/mL}$, and compounds **11a** and **11l** showed inhibition ratios of up to 90% against *R. solani*. Most of the title compounds exhibited moderate nematocidal activities. In general, the morpholine ring may be replaced by other amines and a chlorine atom in the pyridine ring is helpful to fungicidal activity.

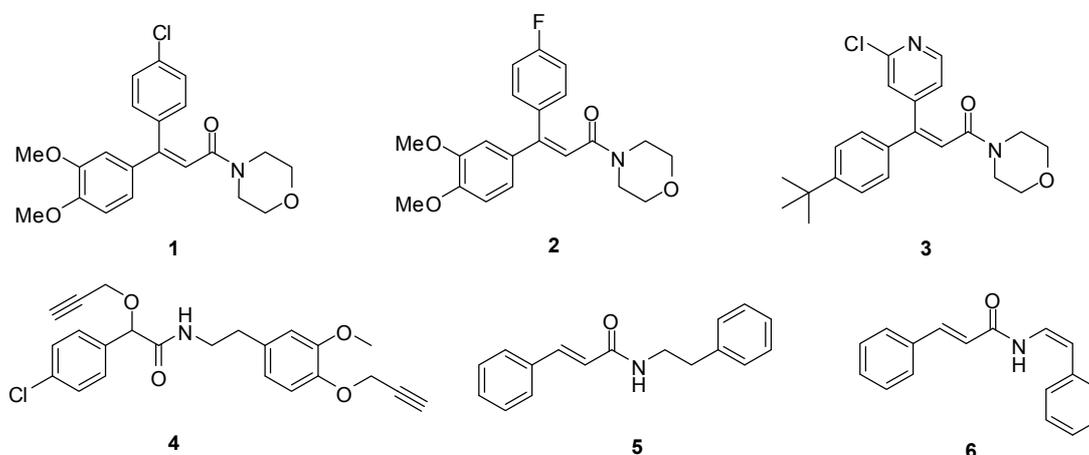
Keywords: cinnamide; β -phenyl ethylamine; fungicidal activity; insecticidal activity

1. Introduction

Cinnamides constitute an important class of compounds with a variety of biological properties, such as nervous central system depressant, anticonvulsant, muscle relaxant, antiallergic, antineoplastic and anti-infective activities, *etc.* [1-7]. In the agrochemical field, their avian repellent, fungicidal and herbicidal activities have also attracted the attention of many researchers [8,9], and several excellent

cinnamide fungicides, for example dimethomorph (**1**) [10], fluormorph (**2**) [11] and pyrimorph (**3**) [12,13], have been successfully developed. Pyrimorph, containing a morpholine ring and a pyridine ring, is a novel fungicide developed by our lab that exhibited excellent activity against oomycetes [14,15]. β -phenylethylamines are also very important bioactive molecules that can be found in many natural and synthetic drugs. Mandipropamide (**4**), which controls foliar diseases caused by oomycetes, is a typical representative of β -phenylethylamines derivatives used in agrochemistry [16,17]. Wan *et al.* have reported the fungicidal activity of (*E*)-*N*-2-phenylethyl cinnamide (**5**) [18] and the insecticidal activity of lansiumamide B (**6**) against *B. xylophilus* and *Culex pipiens* have also been disclosed [19,20] (Figure 1).

Figure 1. Several cinnamide and β -phenylethylamine derivatives with fungicide or insecticidal activity.



Considering the important role of the cinnamoyl, pyridine ring and 2-phenylethylamine moieties in pesticides, their combination might result in novel bioactive molecules. In this study, using pyrimorph as lead compound, we have designed and synthesized a novel series of cinnamide derivatives in which the morpholine moiety in pyrimorph was replaced by a phenethylamino group. All of the target compounds were evaluated for fungicidal and nematocidal activity. Some title compounds showed good fungicidal activity at $50 \mu\text{g mL}^{-1}$, and the compound **11b** exhibited an LC_{50} of $113.8 \mu\text{g mL}^{-1}$ against *B. xylophilus*.

2. Results and Discussion

2.1. Synthesis

The synthetic route to the title 20 compounds involves four-step reaction including Wittig-Horner reaction as the key step (Scheme 1). The Wittig-Horner reaction usually gives a mixture of *E/Z* isomers, but the ratio is quite different depending to the structure of substrates, reaction temperature, solvent, catalyst and so on. In our synthetic route, the reaction of compound **8** with ethyl diethoxyphosphinic acetate predominantly generated the more stable *cis*-intermediate **12** rather than the *trans*-form. This is attributed to the fact that in the *cis*-form the electron-rich carbonyl oxygen has a tendency to donate electrons to the electron-deficient pyridine ring, which leads to the formation of the more stable

intermediate and the *cis*-product **9**. The deduction was confirmed by the crystal structure of **11b**, which was determined by X-ray diffraction analysis (Figure 2 and Table 1).

It can be seen from Figure 1 that the carbonyl and the pyridine ring bearing a chlorine atom are oriented towards the same side, so we can conclude that compound **11b** is the *Z*-isomer.

Scheme 1. Synthetic route to the title compounds **11**.

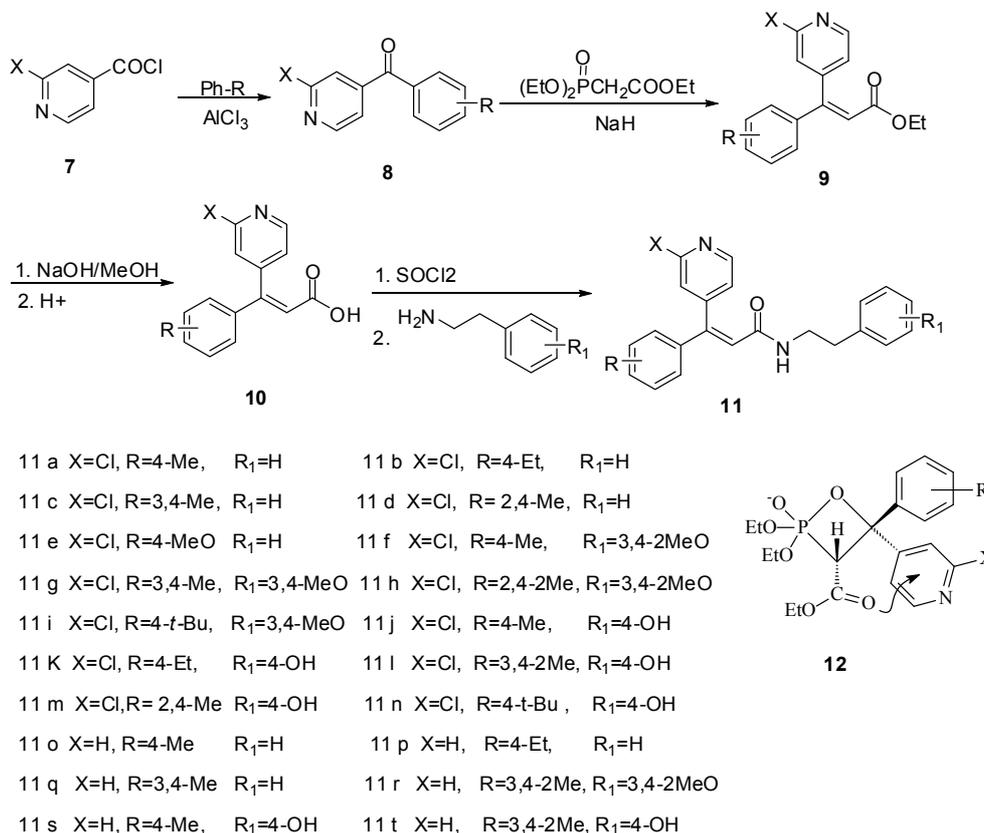


Figure 2. Crystal structure of **11b**.

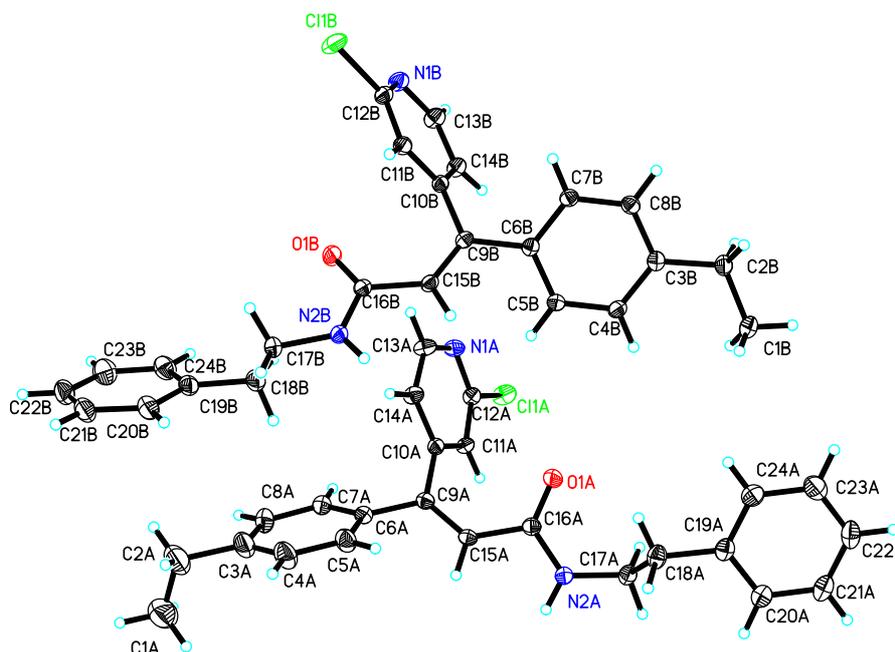


Table 1. Crystal structure and data refinement parameters.

Compound	11b
Empirical formula	C ₂₄ H ₂₃ ON ₂ C
Formula weight	391.2
Crystal system/space group	Triclinic, P-1
Orthorhombic	
a / Å	8.6568(17)
b / Å	13.927(3)
c / Å	18.507(4)
α / °	90°
β / °	90°
γ / °	90°
V / Å ³	2056.1(7)
Z	4
D calc (g/cm ³)	1.263
μ (mm ⁻¹)	0.202
Crystal size (mm)	0.50 × 0.36 × 0.36
Color/shape	Colorless/ rectangle
Temp (K)	173(2)K
Theta range for collection	2.39 < θ < 25.00°
Reflections collected	20946
Independent reflections	7232
Data/restraints/parameters	7232 / 0 / 505
Goodness of fit on F ²	1.062
Final R indices [I > 2 σ (I)]	R ₁ = 0.0481, wR ₂ = 0.1187
R indices (all data)	R ₁ = 0.0514, wR ₂ = 0.1213
Largest difference peak/hole	0.686 and -0.312 e.Å ⁻³

2.2. Biological Activity

The fungicidal activity of the target compounds was tested *in vitro* against seven kinds of common plant pathogens including *R. solani*, *P. parasitica*, *B. cinerea*, *S. sclerotiorum*, *V. mali*, *P. asparagi* and *C. lindemuthianum*). As shown in Table 2, most of the title compounds at 50 $\mu\text{g}\cdot\text{mL}^{-1}$ indicated moderate to high activity in the initial screening against the tested pathogens except *P. parasitica* and *V. mali*, and the inhibition ratios of **11a** and **11l** reached 90% against *R. solani*. The antifungal activity is basically in the following order: **11a** > **11o**, **11b** > **11p**, **11c** > **11q**, **11g** > **11r**, **11j** > **11s**, **11l** > **11t**. That is to say, compounds bearing a chlorine atom in the pyridine ring indicated higher inhibition rates against the seven fungi than those with no chlorine atom in the ring. The results also showed that the morpholine ring of the lead compound pyrimorph could be replaced by β -phenylethylamine.

As structural analogs of lansiumamide B (**6**), the nematocidal activity of title compounds was tested against *Bursaphelenchus xylophilus*. The data is presented in the form of mean mortality and corrected mortality (%) in Table 3. Next, the LD₅₀ of compounds **11b**, **11c** and **11f** were determined and the results are listed in Table 4.

The results of Tables 3 and 4 indicated that the twenty novel cinnamide derivatives displayed moderate insecticidal activity. Compound **11b** indicated the highest nematocidal activity, and the LC₅₀ is 113.8 µg mL⁻¹ against *B. xylophilus*. Compounds **11m** and **11q** also exhibited good mortality.

Table 2. Fungicidal activity of the title compounds (inhibition rate, %).

Compd.	<i>R.</i>	<i>P.</i>	<i>B.</i>	<i>S.</i>	<i>V.</i>	<i>P.</i>	<i>C.</i>
	<i>solani</i>	<i>parasitica</i>	<i>cinerea</i>	<i>sclerotiorum</i>	<i>mali</i>	<i>asparagi</i>	<i>lindemuthianum</i>
11a	93.88	24.41	44	37	48	59.70	59.7
11b	22.45	26.77	50	44	20	34.33	34.33
11c	76.77	1.61	67	72	52	35.82	55.97
11d	4.52	11.29	43	24	31	22.39	47.01
11e	13.55	-2.42	55	42	-6.3	31.34	43.28
11f	82.58	0	59	42	42	39.55	55.22
11g	23.81	14.17	33	28	36	23.88	23.88
11h	35.48	22.58	40	68	29	29.10	42.54
11i	14.84	-8.06	48	53	18	23.13	22.39
11j	72.9	-18.5	33	29	29	55.22	16.42
11k	67.74	28.23	37	17	24	32.09	24.63
11l	90.97	-18.5	54	44	-6.3	17.16	35.82
11m	13.55	-25	38	27	26	42.54	21.64
11n	9.03	-13.7	50	29	-7.8	32.84	39.55
11o	15.48	-17.7	43	16	36	44.03	32.84
11p	9.68	5.65	48	45	30	28.36	37.31
11q	3.87	-9.68	15	2.7	18	23.88	17.16
11r	5.81	-14.5	52	11	68	16.42	28.36
11s	10.32	-17.7	47	5.3	-2.3	28.36	28.36
11t	16.13	14.52	64	27	-2.3	55.97	38.81
pyrimorph	97.20	-	-	79	-	66.50	-
carbendazim	100	14.52	38	100	100		82.09
chlorothalonil	75.48	63.71	95	70	88	82.09	
azoxystrobin	89.03	37.9	80	100	92		

Table 3. Nematicidal Activity of the title compounds.

Compd.	24 h		48 h		72 h	
	Mortality (%)	Corrected mortality (%)	Mortality (%)	Corrected mortality (%)	Mortality (%)	Corrected mortality (%)
11a	21.67 ± 1.67	15.80 ± 1.79	5.00 ± 1.15	28.13 ± 1.28	45.00 ± 1.89	35.35 ± 0.39
11b	23.67 ± 0.88	17.95 ± 0.95	33.33 ± 1.67	26.29 ± 1.84	72.67 ± 1.20	67.87 ± 1.41
11c	20.67 ± 0.67	14.73 ± 0.72	29.00 ± 1.08	21.49 ± 1.30	53.33 ± 1.40	45.15 ± 1.82
11d	28.33 ± 1.20	22.97 ± 1.29	31.67 ± 1.67	24.44 ± 1.84	38.67 ± 1.86	27.91 ± 1.18
11e	19.67 ± 0.33	13.65 ± 0.36	44.67 ± 1.20	38.82 ± 1.33	50.67 ± 2.96	42.01 ± 1.48
11f	19.33 ± 0.67	13.29 ± 0.72	44.33 ± 0.88	38.45 ± 0.97	52.33 ± 1.33	43.97 ± 1.71
11g	15.00 ± 0.00	8.63 ± 0.00i	25.67 ± 1.33	17.81 ± 1.58	33.33 ± 0.88	21.64 ± 1.03
11h	24.67 ± 1.67	19.02 ± 1.87	40.33 ± 0.88	34.02 ± 0.98	47.00 ± 1.45	38.09 ± 1.71
11i	11.00 ± 0.57	4.33 ± 0.62	44.67 ± 0.67	38.82 ± 0.74	53.33 ± 1.67	45.15 ± 1.96
11j	14.00 ± 1.53	7.56 ± 1.64	21.00 ± 0.58	12.65 ± 0.64	27.00 ± 1.15	14.20 ± 1.36

Table 3. Cont.

Compd.	24 h		48 h		72 h	
	Mortality (%)	Corrected mortality (%)	Mortality (%)	Corrected mortality (%)	Mortality (%)	Corrected mortality (%)
11k	20.67 ± 0.67	14.73 ± 0.72	40.00 ± 1.15	33.60 ± 1.28	52.33 ± 1.45	43.97 ± 1.71
11l	10.67 ± 0.33	3.97 ± 0.36	23.00 ± 1.00	14.86 ± 1.11	35.33 ± 1.60	23.99 ± 1.06
11m	18.33 ± 1.02	12.22 ± 1.18	50.00 ± 1.15	44.71 ± 1.28	61.00 ± 1.08	54.16 ± 1.44
11n	26.67 ± 0.67	21.17 ± 0.95	34.67 ± 1.45	27.76 ± 1.61	41.67 ± 1.67	31.44 ± 1.96
11o	15.67 ± 0.67	9.34 ± 0.92	23.00 ± 1.00	14.86 ± 1.11	30.33 ± 0.33	18.11 ± 0.39
11p	14.00 ± 1.00	7.56 ± 1.07	17.00 ± 1.53	8.23 ± 1.69	22.33 ± 0.88	8.71 ± 1.04
11q	33.67 ± 0.88	28.70 ± 0.95	52.67 ± 1.20	47.67 ± 1.32	65.67 ± 1.67	49.07 ± 1.96
11r	1.67 ± 0.88	13.65 ± 0.95	24.33 ± 1.20	16.33 ± 1.33	31.33 ± 0.67	19.29 ± 0.79
11s	14.67 ± 1.45	8.27 ± 1.56	24.67 ± 1.45	16.70 ± 1.61	31.33 ± 1.33	19.29 ± 0.79
11t	18.00 ± 1.15	11.86 ± 1.24	30.00 ± 1.52	22.60 ± 1.78	42.33 ± 1.45	32.22 ± 1.71
6	100.00±0.00	100.00±0.00	100.00±0.00	100.00±0.00	100.00±0.00	100.00±0.00
CK	6.97 ± 1.06 ²		9.50 ± 1.05 ²		13.02 ± 0.88 ²	

Note. The corrected mortality = an average value ± standard error, which is the result after 72 hours of administration. In this column, the same character means no prominent difference at 5% level (LSD).

Table 4. Toxicity of selected compounds against *Bursaphelen-chus xylophilus*at.

Time	Compd.	Regression equation	Correlation coefficient	LD ₅₀ (mg/L)	95% Confidence limit (mg/L)
24 h		Y = 0.41 + 1.85x	0.99	300.56	241.33–373.00
48 h	11b	Y = 0.14 + 2.17x	0.99	173.77	165.11–182.88
72 h		Y = 0.59 + 2.14x	0.99	113.79	95.27–135.90
24 h		y = 0.15 + 1.84x	0.97	429.66	285.32–646.99
48 h	11c	y = 0.02 + 2.00x	0.98	314.58	231.32–429.57
72 h		y = 0.37 + 1.92x	0.95	252.36	170.43–373.67
24 h		y = 0.74 + 1.71x	0.98	305.34	232.32–401.02
48 h	11f	y = 1.89 + 1.38x	0.98	178.50	139.51–228.41
72 h		y = 2.28 + 1.30x	0.94	126.18	80.47–180.78
24 h		y = 0.26 + 5.70x	0.96	8.38	7.77–9.03
48 h	6	y = 0.44 + 5.67x	0.95	6.36	5.90–6.84
72 h		y = 0.62 + 6.00x	0.96	5.38	4.96–5.78
24 h		y = 2.58 + 1.75x	0.94	18.88	10.56–33.75
48 h	Avermec tins	y = 3.35 + 1.73x	0.98	8.98	8.30–9.73
72 h		y = 3.27 + 2.00x	0.99	7.23	6.43–8.12

3. Experimental

3.1. General: Instruments and Methods

The melting points were determined on an XT-4 microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and are uncorrected. ¹H-NMR spectra were obtained at 300 MHz

using a Bruker Avance DPX 300 spectrometer in CDCl₃ or DMSO-d₆ solution, with tetramethylsilane as the internal standard. Chemical-shift values (δ) were given in parts per million (ppm). Mass spectra were obtained at Agilent 1100 series LC/MSD Trap. IR spectra data (cm⁻¹) were determined on VECTOR2 (KBr). The determination of unit cell and data collection was performed on a Rigaku raxis Rapid IP Area Detector by using a graphite-monochromatized diffraction meter with MoK α radiation. Elemental analyses were carried out on an Elementar Vario EL instrument. All analytically pure reagents were purchased from Bailingwei or Beijing Chemical Reagent Co., and the solvents were dried by standard methods in advance and distilled before use.

3.2. General Synthetic Procedures for the Preparation of Compounds 10a–10j

A mixture of 70% sodium hydride (15 mmol) and tetrahydrofuran (THF, 10 mL) was added dropwise to the solution of ethyl diethoxyphosphinic acetate in THF (3 mL, 10 mmol) at 0 °C under stirring. After the evolution of hydrogen ceased, compound **9** in THF (6 mL, 5 mmol) was added dropwise and the mixture was stirred at r.t. for a further 10 h. Water (30 mL) was added slowly and the mixture was extracted with ethyl acetate (10 mL \times 4). The combined organic phase was washed with water, dried with anhydrous magnesium sulphate, filtered, and evaporated to dryness *in vacuo* to give ethyl 3-(pyrid-4-yl)cinnamate as a colorless oil. The oil was dissolved in methanol (30 mL) and NaOH solution (7.5 mL, 2 mol/L), and was stirred at r.t. for further 10 h. The reaction mixture was evaporated to remove the solvent *in vacuo*, and the mixture was extracted twice with ethyl ether (20 mL) after water (40 mL) was added. The aqueous layer was then acidified to pH 2-3 and extracted with ethyl ether (20 mL \times 3) again. The combined organic phase was treated successively by washing with water, drying with anhydrous Na₂SO₄, filtering, evaporating to dryness and recrystallizing from glacial HOAc, to give compounds **10** as white powders.

3-(2-Chloropyridin-4-yl)-3-p-tolylacrylic acid (10a), C₁₅H₁₂O₂NCl, X = Cl, R = 4-Me). Yield 91%, Mp. 191~192 °C. ¹H-NMR (CDCl₃), δ 2.30 (s, 3H, CH₃), 6.50 (s, 1H, =CH), 7.17–7.34 (m, 6H, Ar-H), 8.38(d, *J* = 5.07 Hz, 1H, pyridine-H), 12.36 (brs, 1H, OH).

3-(2-Chloropyridin-4-yl)-3-(4-ethylphenyl) acrylic acid (10b), C₁₆H₁₄O₂NCl, X = Cl, R = 4-Et). Yield 72%, Mp. 152~153 °C. ¹H-NMR (CDCl₃), δ 1.21 (m, 3H, 2CH₃), 2.59 (m, 2H, CH₂), 6.50 (s, 1H, =CH), 7.08–7.35 (m, 6H), 8.38–8.44 (m, 1H, pyridine-H), 12.40 (brs, 1H, OH).

3-(2-Chloropyridin-4-yl)-3-(3,4-dimethylphenyl) acrylic acid (10c), C₁₆H₁₄O₂NCl, X = Cl, R = 3,4-Me). Yield 96%, Mp. 201~202 °C. ¹H-NMR (CDCl₃), δ 2.20 (s, 6H,), 6.61 (s, 1H, =CH), 6.98–7.17 (m, 3H, Ph-H), 7.81–7.83 (dd, 2H, pyridine-H), 8.89 (d, *J* = 1.29 Hz, 1H, pyridine-H), 8.92 (s, 1H, OH).

3-(2-Chloropyridin-4-yl)-3-(2,4-dimethylphenyl) acrylic acid (10d), C₁₆H₁₄O₂NCl, X = Cl, R = 2,4-Me). Yield 85%, Mp. 189~191 °C. ¹H-NMR (CDCl₃), δ 2.10 (s, 3H, CH₃), 2.13 (s, 3H, CH₃), 6.63 (s, 1H, =CH), 6.98 (d, *J* = 2.03 Hz, 1H), 7.01–7.18 (m, 4H, Ph-H), 7.84 (dd, 2H, pyridine-H), 8.75 (d, *J* = 3.57 Hz, 1H), 12.38 (brs, 1H, OH).

3-(2-Chloropyridin-4-yl)-3-(4-methoxyphenyl) acrylic acid (10e), C₁₆H₁₄O₃NCl, X = Cl, R = 4-OMe). Yield 68%, Mp. 168~170 °C. ¹H-NMR(CDCl₃), δ 3.80 (s, 3H, CH₃), 6.51 (s, 1H, =CH), 7.06–7.22 (m,

4H, Ph-H), 7.40 (dd, 2H, Pyridine-H), 8.75 (d, $J = 3.57$ Hz, 1H, Pyridine-H), 12.46 (brs, 1H, OH).

3-(4-tert-Butylphenyl)-3-(2-chloropyridin-4-yl)-acrylic acid (10f), $C_{17}H_{16}O_2NCl$, X = Cl, R = 4-*t*-Bu). Yield 55%, Mp. 176–177 °C. 1H -NMR($CDCl_3$), δ 1.32 (s, 9H, 3CH₃), 6.23 (s, 1H, =CH), 7.08–7.20 (m, 4H, Ph-H), 7.40 (dd, 2H, Pyridine-H), 8.45 (d, $J = 5.01$ Hz, 1H, Pyridine-H), 12.36 (brs, 1H, OH).

*3-(Pyridin-4-yl)-3-*p*-tolylacrylic acid (10g)*, $C_{15}H_{13}O_2N$, X = H, R = 4-Me). Yield 83%, Mp. 221–222 °C. 1H -NMR ($CDCl_3$), δ 2.40 (s, 3H, CH₃), 6.48 (s, 1H, =CH), 7.09–7.23 (m, 6H, Ar-H), 8.55–8.60 (m, 2H, pyridine-H), 11.89 (brs, 1H, OH).

3-(4-Ethylphenyl)-3-(pyridin-4-yl)-acrylic acid (10h), $C_{16}H_{15}O_2N$, X = H, R = 4-Et). Yield 59%, Mp. 205–206 °C. 1H -NMR ($CDCl_3$), δ 1.14–1.25 (m, 3H, CH₃), 2.50–2.67 (m, 2H, CH₂), 6.48 (s, 1H, =CH), 6.90–7.14 (m, 4H), 7.20–7.25 (m, 2H), 11.89 (brs, 1H, OH).

3-(3,4-Dimethylphenyl)-3-(pyridin-4-yl)acrylic acid (10i), $C_{16}H_{15}O_2N$, X = H, R = 3,4-Me). Yield 77%, Mp. 238–240 °C. 1H -NMR ($CDCl_3$), δ 2.20 (d, $J = 14.55$ Hz, 3H, CH₃), 2.27 (d, $J = 3.54$ Hz, 3H, CH₃), 6.48 (s, 1H, =CH), 6.90–7.14 (m, 3H, Ph-H), 7.20–7.25 (m, 2H, pyridine-H), 8.52–8.58 (m, 2H, pyridine-H), 11.90 (brs, 1H, OH).

3-(2,4-Dimethylphenyl)-3-(pyridin-4-yl) acrylic acid (10j), $C_{16}H_{15}O_2N$, X = H, R = 2,4-2Me). Yield 62%, Mp. 207–208 °C. 1H -NMR ($CDCl_3$), δ 2.05 (s, 3H, CH₃), 2.33 (s, 3H, CH₃), 6.20 (s, 1H, =CH), 7.00–7.08 (m, 3H, Ph-H), 7.30 (dd, 2H, pyridine-H), 8.52 (dd, 2H, pyridine-H), 9.99 (brs, 1H, OH).

3.3. General Synthetic Procedures for Compounds 11a–11t

Thionyl chloride (6.95 mmol) was added dropwise to the mixture of compound **10** (3.66 mmol) and DMF of catalytic amount in CH_2Cl_2 (20 mL) and then stirred continuously for eight hours at 0 °C. The reaction mixture was evaporated to remove the solvent and excess thionyl chloride *in vacuo* and the residue was dissolve using CH_2Cl_2 (20 mL). β -Phenylethamine (4.13 mmol) and triethylamine (catalytic amount) in CH_2Cl_2 (10 mL) was added to the residue at 0 °C. The reaction mixture was stirred at r.t. for further 10 h, and then was washed with hydrogen chloride (1 mol/L), saturated potassium carbonate solution and water, dried over anhydrous $MgSO_4$, and concentrated to give the crude product. Recrystallization from methanol afforded the title compounds.

*3-(2-Chloropyridin-4-yl)-*N*-phenethyl-3-*p*-tolylacrylamide (11a)*, X = Cl, R = 4-Me, R₁ = H), Yield 59%, Mp. 158–160 °C, 1H -NMR ($CDCl_3$), δ 2.35 (s, 3H, CH₃), 2.74 (t, 2H, CH₂), 3.51(q, 2H, CH₂), 5.60 (brs, 1H, NH), 6.28 (s, 1H, =CH), 7.04–7.33 (m, 11H, Ar-H), 8.37 (dd, 1H, $J = 6.87, 6.40$ Hz, pyridine-H). MS m/z (ESI) 377.2 $[M+H]^+$ Anal. Calc. for $C_{23}H_{21}ON_2Cl$ (376.13): C, 73.30; H, 5.62; N, 7.43; found: C, 73.22; H, 5.62; N, 7.50.

*3-(2-Chloropyridin-4-yl)-3-(4-ethylphenyl)-*N*-phenethylacrylamide (11b)*, X = Cl, R = 4-Et, R₁ = H). Yield 88%, Mp. 142–143 °C, 1H -NMR ($CDCl_3$), δ 1.23 (t, 3H, CH₃), 2.65 (q, 2H, CH₂), 2.74 (t, 2H, CH₂), 3.50 (q, 2H, CH₂), 5.60 (brs, 1H, NH), 6.29 (s, 1H, =CH), 7.07–7.33 (m, 11H, Ar-H), 8.37 (dd, $J = 6.78, 6.39$ Hz, 1H, pyridine-H). MS m/z (ESI) 391.2 $[M+H]^+$. Anal. Calc. for $C_{24}H_{23}ON_2Cl$ (390.15): C, 73.74; H, 5.93; N, 7.17; found C, 73.61; H 5.84; N 7.24.

3-(2-Chloropyridin-4-yl)-3-(3,4-dimethylphenyl)-N-phenethylacrylamide (11c, X = Cl, R = 3,4-Me, R₁ = H). Yield 93%, Mp. 162–163 °C, ¹H-NMR(CDCl₃), δ 2.21 (q, 3H, CH₃), 2.26 (t, 3H, CH₃), 2.74 (t, 2H, CH₂), 3.50 (q, 2 H, CH₂), 5.60 (brs, 1H, NH), 6.28 (s, 1H, =CH), 6.87–7.33 (m, 10H, Ar-H), 8.33 (dd, *J* = 6.63, 6.81 Hz, 1H, pyridine-H). MS *m/z* (ESI) 391.2 [M+H]⁺. Anal. Calc. For C₂₄H₂₃ON₂Cl (390.15): C, 73.73; H, 5.93; N 7.17; found: C 73.74; H, 5.93; N, 7.20.

3-(2-Chloropyridine-4-yl)-3-(2,4-dimethylphenyl)acrylamide (11d, X = Cl, R = 2,4-2Me, R₁ = H). Yield 68%, Mp. 160–161 °C, ¹H-NMR (CDCl₃), δ2.01 (q, 3H, CH₃), 2.30 (t, 3H, CH₃), 2.77 (t, 2H, CH₂), 3.53 (q, 2H, CH₂), 5.45 (brs, 1H, NH), 6.05 (s, 1H, =CH), 6.98–7.32 (m, 10H, Ar-H), 8.33 (dd, *J* = 7.5, 7.5 Hz, 1H, pyridine-H). MS *m/z* (ESI) 391.20 [M+H]⁺. Anal. Calc. for C₂₄H₂₃ON₂Cl (390.15): C, 73.74; H 5.93; N, 7.17; found: C, 73.72; H, 5.93; N, 7.22.

3-(2-Chloropyridin-4-yl)-3-(4-methoxyphenyl)-N-phenethylacrylamide (11e, X = Cl, R = 4-MeO, R₁ = H). Yield 71%, Mp. 185–186 °C, ¹H-NMR (CDCl₃), δ2.74 (t, 2H, CH₂), 3.50 (q, 2H, CH₂), 3.80 (s, 3H, CH₃O), 5.45 (brs, 1H, NH), 6.24 (s, 1H, =CH), 6.83–7.33 (m, 11H, Ar-H), 8.37 (dd, *J* = 5.70, 5.67 Hz, 1H, pyridine-H). MS *m/z* (ESI) 393.13[M+H]⁺. Anal. Calc. for C₂₃H₂₁O₂N₂Cl (392.13): C, 70.71; H, 5.39; N, 7.13; found : C, 70.32; H, 5.34; N, 7.20.

3-(2-Chloropyridin-4-yl)-N-(3,4-dimethoxyphenethyl)-3-p-tolylacrylamide (11f, X = Cl, R = 4-Me, R₁ = 3,4-MeO). Yield 77%, Mp. 181–182 °C, ¹H-NMR (CDCl₃), δ2.30 (t, 3H, CH₃), 2.36 (q, 2H, CH₂), 3.21 (q, 2H, CH₂), 3.71 (s, 3H, CH₃O), 3.73 (s, 3H, CH₃O), 6.58 (s, 1H, =CH), 6.67–7.25 (m, 9H, Ar-H), 8.23 (brs, 1H, NH), 8.38 (dd, *J* = 6.54, 6.54 Hz, 1H, pyridine-H). MS *m/z* (ESI) 437.2 [M+H]⁺. Anal. Calc. for C₂₅H₂₅O₃N₂Cl (436.16): C, 68.72; H, 5.77; N, 6.41; found: C, 68.30, H, 5.78; N, 6.35.

3-(2-Chloropyridin-4-yl)-N-(3,4-dimethoxyphenethyl)-3-(3,4-dimethylphenyl)acrylamide (11g, X = Cl, R = 3,4-Me, R₁ = 3,4-MeO). Yield 81%, Mp. 157–159 °C, ¹H-NMR (CDCl₃), δ2.20 (s, 3H, CH₃), 2.26 (s, 3H, CH₃), 2.68 (t, 2H, CH₂), 3.52 (q, 2H, CH₂), 3.85 (s, 3H, CH₃O), 3.87 (s, 3H, CH₃O), 5.50 (brs, 1H, NH), 6.28 (s, 1H, =CH), 6.62–7.18 (m, 8H, Ar-H), 8.38 (dd, *J* = 5.4, 4.8 Hz, 1H, pyridine-H). MS *m/z* (ESI) 451.2 [M+H]⁺. Anal. Calc. for C₂₆H₂₇O₃N₂Cl (450.17): C, 69.25; H, 6.03; N, 6.21; found,: C, 69.01; H, 5.99; N, 6.20.

3-(2-Chloropyridin-4-yl)-N-(3,4-dimethoxyphenethyl)-3-(2,4-dimethylphenyl)acrylamide (11h, X = Cl, R = 2,4-Me, R₁ = 3,4-MeO). Yield 77%, Mp. 111–113 °C, ¹H-NMR (CDCl₃), δ1.99 (d, 3H, CH₃), 2.02 (d, 3H, CH₃), 2.34 (t, 2H, CH₂), 3.51 (q, 2H, CH₂), 3.84 (s, 3H, CH₃O), 3.85 (s, H, CH₃O), 5.50 (brs, 1H, NH), 6.05 (s, 1H, =CH), 6.58–7.14 (m, 8H, Ar-H), 8.39 (dd, *J* = 6.18, 6.39 Hz, 1H, pyridine-H). MS *m/z* (ESI) 451.2 [M+H]⁺. Anal. Calc. for C₂₆H₂₇O₃N₂Cl (450.17): C, 69.25; H, 6.03; N, 6.21; found: C, 69.10; H, 6.03; N, 6.20.

*3-(4-tert-Butylphenyl)-3-(2-chloropyridin-4-yl)-N-(3,4-dimethoxyphenethyl)acrylamide (11i, X=Cl, R=4-*t*-Bu, R₁ = 3,4-2MeO)*. Yield 53%, Mp. 146–148 °C, ¹H-NMR (CDCl₃), δ1.33 (t, 9H, C(CH₃)₃), 2.70 (t, 2H, CH₂), 3.48 (q, 2H, CH₂), 3.84 (s, 3H, CH₃O), 3.86 (s, 3H, CH₃O), 5.50 (brs, 1H, NH), 5.57 (t, 1 H, =CH), 6.63–7.38 (m, 9H, Ar-H), 8.38 (dd, *J* = 7.02, 6.93 Hz, 1H, pyridine-H). MS *m/z* (ESI)

479.20[M+H]⁺. Anal. Calc. for C₂₈H₃₁O₃N₂Cl (478.20): C, 70.21; H, 6.52; N, 5.85; found: C, 69.90; H, 6.50; N, 5.90.

3-(2-Chloropyridin-4-yl)-N-(4-hydroxyphenethyl)-3-p-tolylacrylamide (**11j**, X = Cl, R = 4-Me, R₁ = 4-OH). Yield 94%, Mp. 233–234 °C, ¹H-NMR (DMSO), δ 2.30 (s, 3H, CH₃), 2.36 (s, 3H, CH₃), 2.51 (t, 2H, CH₂), 3.21 (t, 2H, CH₂), 6.56 (s, 1H, =CH), 6.63–7.29 (m, 8H, Ar-H), 7.17–7.30 (m, 2H, pyridine-H), 8.07 (brs, 1H, NH), 8.38 (d, *J* = 5.25 Hz, 1H, pyridine-H), 9.18 (brs, 1H, OH). MS *m/z* (ESI) 391.2 [M-H]⁺ Anal. Calc. for C₂₃H₂₁O₂N₂Cl (392.13): C, 70.31; H, 5.39; N, 7.13; found: C, 69.95; H, 5.33; N, 7.16.

3-(2-Chloropyridin-4-yl)-3-(4-ethylphenyl)-N-(4-hydroxyphenethyl)acrylamide (**11k**, X = Cl, R = 4-Et, R₁ = 4-OH). Yield 88%, Mp. 231–232 °C, ¹H-NMR (DMSO), δ 1.15–1.23 (m, 3H, CH₃), 2.45–2.52 (m, 2H, CH₂), 2.60–2.67 (m, 2H, CH₂), 3.15–3.22 (m, 2H, CH₂), 6.64 (s, 1H, =CH), 6.65–7.29 (m, 8H, Ar-H), 7.17–7.30 (m, 2H, pyridine-H), 8.06 (brs, 1H, NH), 8.38 (d, *J* = 5.25 Hz, 1H, pyridine-H) 9.18 (s, 1 H, OH). MS *m/z* (ESI) 405.20 [M-H]⁺ Anal. Calc. for C₂₄H₂₃O₂N₂Cl (406.14): C, 70.84; H, 5.70; N, 6.88; found: C, 70.57; H, 5.70; N, 6.81.

3-(2-Chloropyridin-4-yl)-3-(3,4-dimethylphenyl)-N-(4-hydroxyphenethyl)acrylamide (**11l**, X = Cl, R = 3,4-Me, R₁ = 4-OH). Yield 95%, Mp. 159–161 °C, ¹H-NMR (DMSO), δ 2.27 (s, 3H, -CH₃), 2.30 (s, 3H, -CH₃), 2.51 (t, 2H, -CH₂), 3.19 (t, 2H, -CH₂), 5.76 (s, 1H, =CH), 6.54–7.21 (m, 9H, Ar-H), 8.21 (brs, 1H, -NH), 8.36 (d, 1H, *J* = 5.07 Hz, pyridine-H), 9.18 (brs, 1H, OH). MS *m/z* (ESI) 405.3 [M-H]⁺ Anal. Calc. for C₂₄H₂₃O₂N₂Cl (406.14): C, 70.84; H, 5.70; N, 6.88; found: C, 70.59; H, 5.70, N, 6.78.

3-(2-Chloropyridin-4-yl)-3-(2,4-dimethylphenyl)-N-(4-hydroxyphenethyl)acrylamide (**11m**, X = Cl, R = 2,4-Me, R₁ = 4-OH). Yield 89%, Mp. 244–246 °C, ¹H-NMR (DMSO), δ 2.04 (s, 6H, -CH₃), 2.56 (t, 2H, -CH₂), 3.21 (t, 2H, -CH₂), 6.14 (s, 1H, =CH), 6.66–7.19 (m, 9H, Ar-H), 8.26 (brs, 1H, -NH), 8.31 (dd, *J* = 5.4, 5.1 Hz, 1 H, pyridine-H), 9.10 (brs, 1H, -OH). MS *m/z* (ESI) 405.1 [M-H]⁺. Anal. Calc. for C₂₄H₂₃O₂N₂Cl (406.14): C, 70.84; H, 5.70; N, 6.88; found: C, 70.53; H, 5.60; N, 6.79.

3-(4-tert-Butylphenyl)-3-(2-chloropyridin-4-yl)-N-(4-hydroxyphenethyl)acrylamide (**11n**, X = Cl, R = 4-*t*-Bu, R₁ = 4-OH). Yield 45%, Mp. 205–207 °C, ¹H-NMR (DMSO), δ 1.28 (s, 9H, 3CH₃), 2.50 (t, 2H, CH₂), 3.21 (t, 2H, CH₂), 6.57 (s, 1H, =CH), 6.63–7.95 (m, 10H, Ar-H), 8.23 (brs, 1H, NH), 8.37 (dd, *J* = 6.90, 6.60 Hz, 1H, pyridine-H), 9.19 (brs, 1H, OH). MS *m/z* (ESI) 433.20 [M-H]⁺. Anal. Calc. for C₂₆H₂₇O₂N₂Cl (434.18): C, 71.80; H, 6.26; N, 6.44; found: C, 71.54; H, 6.03; N, 6.21.

N-phenethyl-3-(pyridin-4-yl)-3-p-tolylacrylamide (**11o**, X = H, R = 4-Me, R₁ = H). Yield 58%, Mp. 191–192 °C, ¹H-NMR (DMSO), δ 2.35 (s, 3H, CH₃), 2.70 (t, 2H, -CH₂), 3.46 (m, 2H, -CH₂), 5.42 (brs, 1H, -NH), 6.32 (s, 1H, =CH), 7.06–7.31 (m, 11H, Ar-H), 8.60 (m, 2H, pyridine-H). MS *m/z* (ESI) 343.20[M+H]⁺. Anal. Calc. for C₂₃H₂₂O₂N₂ (342.17): C, 80.67; H, 6.48; N, 8.18; found: C, 80.63; H, 6.46; N, 8.26.

3-(4-Ethylphenyl)-N-phenethyl-3-(pyridin-4-yl)acrylamide (**11p**, X = H, R = 4-Et, R₁ = H). Yield 56%, Mp. 135–137 °C, ¹H-NMR (CDCl₃), δ 1.21 (t, 3H, CH₃), 2.36 (q, 2H, CH₂), 2.63 (t, 2H, CH₂), 3.46 (q, 2H, CH₂), 5.41 (brs, 1H, NH), 6.32 (s, 1H, =CH), 7.06–7.31 (m, 12H, Ar-H), 8.61 (dd, *J* = 1.65, 1.65 Hz,

2H, pyridine-H). MS m/z (ESI) 357.20 $[M+H]^+$. Anal. Calc. for $C_{24}H_{24}ON_2$ (356.19): C, 80.87; H, 6.79; N, 7.86; found: C, 80.73; H, 6.80; N, 7.89.

3-(3,4-Dimethylphenyl)-*N*-phenethyl-3-(pyridin-4-yl)acrylamide (**11q**, X = H, R = 3,4-Me, R₁ = H). Yield 93%, Mp. 182–183 °C, ¹H-NMR (CDCl₃), δ 2.21 (t, 3H, CH₃), 2.36 (q, 3H, CH₃), 2.63 (t, 2H, CH₂), 3.46 (m, 2H, CH₂), 5.41 (brs, 1H, NH), 6.32 (s, 1H, =CH), 7.06–7.31 (m, 11H, Ar-H), 8.54 (dd, $J = 1.59, 1.59$ Hz, 1H, pyridine-H). MS m/z (ESI) 357.20 $[M+H]^+$. Anal. Calc. for $C_{24}H_{24}ON_2$ (356.19): C, 80.87; H, 6.79; N, 7.86; found: C, 80.85; H, 6.78; N, 7.90.

N-(3,4-Dimethoxyphenethyl)-3-(3,4-dimethylphenyl)-3-(pyridin-4-yl)acrylamide (**11r**, X = H, R = 3,4-Me, R₁ = 3,4-2MeO). Yield 85%, Mp. 172–174 °C, ¹H-NMR (CDCl₃), δ 2.21 (t, 3H, CH₃), 2.26 (s, 3H, CH₃), 2.64 (t, 2H, CH₂), 3.43 (q, 2H, CH₂), 3.86 (s, 3H, CH₃O), 3.87 (s, 3H, CH₃O), 5.44 (brs, 1H, NH), 6.31 (s, 1H, =CH), 6.59–7.27 (m, 8H, Ar-H), 8.61 (dd, 2H, $J = 1.53, 1.53$ Hz, 2H, pyridine-H). MS m/z (ESI) 417.30 $[M+H]^+$. Anal. Calc. for $C_{26}H_{28}O_3N_2$ (416.21): C, 74.97; H, 6.78; N, 6.73; found: C, 74.60; H, 6.80; N, 6.63.

N-(4-Hydroxyphenethyl)-3-(pyridin-4-yl)-3-*p*-tolylacrylamide (**11s**, X = H, R = 4-Me, R₁ = 4-OH). Yield 88%, Mp. 244–246 °C, ¹H-NMR (DMSO), δ 2.30 (s, 3H, CH₃), 2.50–2.53 (m, 2H, CH₂), 3.15–3.22 (m, 2H, CH₂), 6.51 (s, 1H, =CH), 6.66–7.20 (m, 11H, Ar-H), 8.14 (brs, 1H, NH), 8.51–8.55 (m, 1H, pyridine-H), 9.19 (brs, 1H, OH). MS m/z (ESI) 356.20 $[M-2H]^+$. Anal. Calc. for $C_{23}H_{22}O_2N_2$ (358.20): C, 77.07; H, 6.19; N, 7.93; found: C, 76.93; H, 6.17; N, 7.71.

3-(3,4-Dimethylphenyl)-*N*-(4-hydroxyphenethyl)-3-(pyridin-4-yl)acrylamide (**11t**, X = H, R = 3,4-Me, R₁ = 4-OH). Yield 96%, Mp. 159–161 °C, ¹H-NMR (DMSO), δ 2.01 (s, 3H, CH₃), 2.11 (s, 3H, CH₃), 2.50–2.53 (t, 2H, CH₂), 3.15–3.22 (q, 2H, CH₂), 6.70 (s, 1H, =CH), 6.66–7.20 (m, 10H, Ar-H), 8.23 (brs, 1H, NH), 8.51–8.55 (m, 1H, pyridine-H), 9.20 (brs, 1H, OH). MS m/z (ESI) 370.20 $[M-2H]^+$. Anal. Calc. for $C_{24}H_{24}O_2N_2$ (372.18): C, 77.39; H, 6.49; N, 7.52; found: C, 77.29; H, 6.44; N, 7.55.

Crystal data can be obtained from the Crystallographic Data Centre as supplementary publication number CCDC 848237. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

3.4. Bioassays

3.4.1. Fungicidal Activity Test

The fungicidal activity of the target compounds against *R. solani*, *P. parasitica*, *B. cinerea*, *S. sclerotiorum*, *V. mali*, *P. asparagi* and *C. lindemuthianum* were evaluated using the mycelium growth rate test [21]. Pyrimorph, carbendazim, chlorothalonil, azoxystrobin were used as controls. Their relative inhibition ratio (%) were calculated as equal to the (colony diameter of control – colony diameter of treatment)/(colony diameter of control – mycelial disks diameter) × 100. This experiment was conducted twice with four replicates.

3.4.2. Nematicidal Activity

All the compounds were dissolved in acetone and diluted to a 200 mg L⁻¹ solution with distilled water. The solution (1.5 mL) was placed in a 24 holes cellplate with nematode solution (0.5 mL, nearly five hundred nematodes of mixed ages), and the plate was put in a culture box at 25 °C. A distilled water test was used as blank control and every test was replicated three times. The mortality of insects was counted after 24, 48 and 72 hours of administration, and Abbotts formula was used to correct the mortality relative to that of negative control.

4. Conclusions

Using pyrimorph as the lead compound, we designed and synthesized twenty novel cinnamamides derivatives using Wittig-Horner reaction as the key step. X-ray data showed that the Wittig-Horner reactions mainly gave the *Z*-isomer product. The preliminary bioassay results demonstrated that most of the title compounds show a wide spectrum of activity against plant pathogens at 50 µg·mL⁻¹. Compounds **11a** and **11l** showed higher fungicidal activity than the other compounds. The title compounds exhibited moderate nematicidal activity. Generally, the morpholine ring might be replaced by other amines and a chlorine atom in the pyridine ring is helpful to fungicidal activity.

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References and Notes

1. Kamal, A.; Balakishan, G.; Ramakrishna, G.; Basha, S.T.; Sreekanth, K.; Balakrishna, M.; Rajender; Dastagiri, D.; Kalivendi, S.V. Synthesis and biological evaluation of cinnamido linked pyrrolo [2,1-c] [1,4]benzodiazepines as antimetabolic agents. *Eur. J. Med. Chem.* **2010**, *45*, 3870-3884.
2. Cai, X.H.; Wu, Y.H. Synthesis and α -glucosidase inhibitory activity of cinnamic amides. *Chin. J. Org. Chem.* **2007**, *27*, 77-81.
3. Kristan, K.; Starcević, S.; Brunskole, M.; Rižner, T.L.; Gobec, S. Cinnamates and cinnamamides inhibit fungal 17 β -hydroxysteroid dehydrogenase. *Mol. Cell Endocrinol.* **2006**, *248*, 239-241.
4. Debnath, B.; Samanta, S.; Roy, K.; Jha, T. QSAR study on some p-arylthio cinnamides as antagonists of biochemical ICAM-1/LFA-1 interaction and ICAM-1/JY-8 cell adhesion in relation to anti-inflammatory activity. *Bioorg. Med. Chem.* **2003**, *11*, 1615-1619.
5. Han, X.B.; Feng, H.J.; Chen, G.R.; Li, Y.C. Syntheses and biological activities of α -substituted N-(phenylethyl)cinnamides. *Chin. J. Med. Chem.* **2003**, *13*, 329-334, 355.
6. Xu, F.; Zhang, S.H.; Shao, R.G.; Zhen, Y.S. Anticancer activity of sodium caffeate and its mechanism. *Acta Pharmacol. Sin.* **2005**, *26*, 1248-1252.
7. Zhen, Y.S.; Jiang, X.F. Cinnamamide, an antitumor agent with low cytotoxicity acting on matrix

- metalloproteinase. *Anti-Cancer Drug*. **2000**, *11*, 49-54.
8. Gill, E.L.; Watkins, R.W.; Cowan, D.P.; Bishop, J.D.; Gurney, J.E. Cinnamamide, an avian repellent, reduces woodpigeon damage to oilseed rape. *Pestic. Sci.* **1998a**, *52*, 159-164.
 9. Gill, E.L.; Feare, C.J.; Cowan, D.P.; Fox, S.M.; Bishop, J.D.; Langton, S.D.; Watkins, R.W.; Gurney, J.E. Cinnamamide modifies foraging behaviors of free-living birds. *J. Wildlife Manage.* **1998b**, *62*, 872-884.
 10. Kuhn, P.J.; Pitt, D.; Lee, S.A.; Wakley, G.; Shepard, A.N. Effects of dimethomorph on the morphology and ultra structure of phytophthora. *Mycol. Res.* **1991**, *95*, 333-340.
 11. Liu, W.C.; Liu, C.L. Novel fungicide flumorph(SYP-L190) with high activity. *Pesticides* **2002**, *41*, 8-11.
 12. Qin, Z.H.; Mu, C.W.; Mao, S.F.; Dong, Y.H.; Li, N.; Zhang, S.S. Preparation of 4-[3-(pyridin-4-yl)-3-phenylacryl]morpholine derivatives as fungicides. CN Patent 1566095, 19 January 2005.
 13. Mu, C.W.; Yuan, H.Z.; Li, N.; Fu, B.; Xiao, Y.M.; Ma, Y.Q.; Qi, S.H.; Qin, Z.H. Synthesis and fungicidal activities of a novel series of 4-[3-(pyrid-4-y1)-3-substituted phenyl acryloyl] morpholine. *Chem. J. Chinese U.* **2007**, *28*, 1902-1906.
 14. Huang, X.Y.; Yuan, H.Z.; Qin, Z.H.; Chen, X.X.; Qi, S.H. Preliminary studies on the mode of action of pyrimorph against phytophthora infestans. *Chin. J. Pestic. Sci.* **2007**, *9*, 376-382.
 15. Yan, X.J.; Qin, W.C.; Sun, L.P.; Qi, S.H.; Yang, D.B.; Qin, Z.H.; Yuan, H.Z. Study of inhibitory effects and action mechanism of the novel fungicide Pyrimorph against *Phytophthora capsici*. *J. Agric. Food Chem.* **2010**, *58*, 2720-2725.
 16. Lamberth, C.; Cederbaum, F.; Jeanguenat, A.; Kempf, H.; Zeller, M.; Zeun, R. Synthesis and fungicidal activity of *N*-2-(3-methoxy-4-propargyloxy) phenethyl amides. Part II: Anti-oomycetic mandelamides. *Pest Manag. Sci.* **2006**, *62*, 446-451.
 17. Su, N.; Wang, Z.J.; Wang, L.Z.; Zhang, X.; Dong, W.L.; Wang H.X.; Li Z.M.; Zhao W.G. Synthesis and biological evaluation of isosteric analogs of mandipropamid for the control of Oomycete pathogens. *Chem. Biol. Drug Des.* **2011**, *78*, 101-111.
 18. Liu, X.M.; Wan, S.Q. The Content of (*E*)-*N*-2-Phenylethylcinnamamide in different organ of clausena lansium and the activity to colletotrchum musae. *Pesticides* **2008**, *47*, 15-16.
 19. Liu, Y.X.; Gong, Z.Y.; Wan, S.Q. Inhibitory effects of clausenamamide alkaloid on seven fruit pathogenic fungi. *Plant Protection* **2009**, *35*, 53-56.
 20. Stefanuti, I.; Smith, S.A.; Taylor, R.J.K. Unsaturated enamides via organometallic addition to isocyanates: The synthesis of Lansamide-I, Lansiumamides A-C and SB-204900. *Tetrahedron Lett.* **2000**, *41*, 3735-3738.
 21. Chen, N.C. *Pesticide Bioassay Method*; Beijing Agriculture University Press: Beijing, China, 1998; p. 12.

Sample Availability: Samples of the compounds 11 are available from the authors.