

Synthesis of 1-Acyl-3-isopropenylbenzimidazolone Derivatives and Their Activity against *Botrytis cinerea*[†]

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A series of 1-acyl-3-isopropenylbenzimidazolone derivatives were synthesized, and their structures were characterized by ¹H and ¹³C NMR and elemental analysis. Their fungicidal activities against *Botrytis cinerea* were also evaluated by spore germination assay. The acrylic acid, methacrylic acid, 4-chlorophenyl acetic acid, and 2-chlorobenzoic acid derivatives exhibited strong fungicidal activity. This implied that benzimidazolones might be potential fungicide leading compounds.

KEYWORDS: Benzimidazolone derivatives; synthesis; fungicidal activities

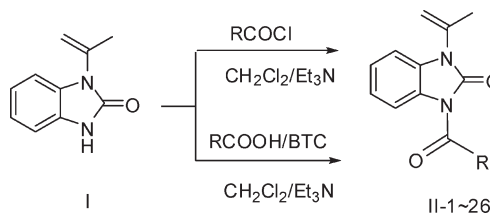
INTRODUCTION

Gray mold, which is caused by *Botrytis cinerea*, is one of the most common diseases on vegetable and fruit crops (1). Its development is dependent upon favorable climatic conditions, and it has been a serious threat in greenhouses when humidity is high and temperature is moderate. Protecting crops against *B. cinerea* requires multiple applications of fungicides, during the whole period from bud burst until ripening. However, with the extensive use of synthetic fungicides, *B. cinerea* has developed resistance to many commercialized products (2, 3).

Benzimidazolone derivatives have been found to exhibit anti-HIV (4), antitrichinellosis (5), antinociceptive (6), antitumor activities (7), and other pharmacological activities (8–11), whereas only a few of them exhibit antimicrobial activities. For example, the benzimidazolone derivative bearing a sugar residue on the aromatic nitrogen effectively inhibits the growth of bacteria such as *Bacillus cereus*, *Streptomyces chartreusis*, and *Escherichia coli* (12). However, to the best of our knowledge, there has been no report on the fungicidal activity of benzimidazolones against plant pathogens.

1-Isopropenylbenzimidazolone (Scheme 1, compound I), which could be prepared by the condensation of *o*-phenylenediamine with acetoacetic ester (13), is often used as the intermediate to synthesize other benzimidazolones (7, 14, 15). In most cases, isopropenyl, playing the role of amine protecting group, was removed or substituted by other groups in the succeeding procedures. In other cases, substituents were introduced to the other nitrogen atom of 1-isopropenylbenzimidazolone. In a recent paper, five sulfonamide derivatives of isopropenylbenzimidazolone were synthesized and their cytotoxicities against several strains of cancer cell evaluated (7). In general, the

Scheme 1



bioactivities of isopropenylbenzimidazolone derivatives were still not thoroughly investigated.

In this paper, we prepared a series of isopropenylbenzimidazolone derivatives; herein the alkyl carbonyl or aromatic carbonyl was introduced to the nitrogen atom by amide bond (Scheme 1, compounds II-1–II-26). Their fungicidal activities against *B. cinerea* were evaluated by the method of spore germination, and several compounds exhibited strong inhibition. Here we report the exciting results. The structure–activity relationship of these benzimidazolone derivatives is also discussed.

MATERIALS AND METHODS

Instruments. The melting points of the products were determined on an X-4 apparatus (Beijing Tech Instrument Co., Beijing, China) and are uncorrected. ¹H and ¹³C NMR spectra were taken on a Bruker Avance 600 MHz (600 MHz for ¹H and 150 MHz for ¹³C, respectively) spectrometer in CDCl₃ solution with TMS as an internal standard. Elemental analyses were carried out on an Elementar Vairo EL analyzer.

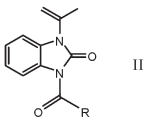
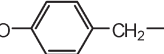
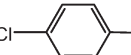
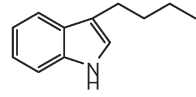
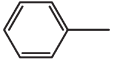
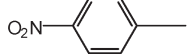
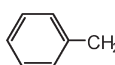
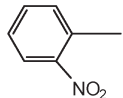
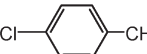
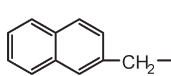
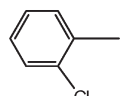
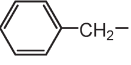
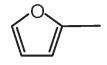
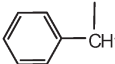
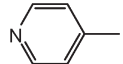
Synthetic Procedures. Isopropenyl benzimidazolone (I) (Zhengzhou Sigma Chemical Co., Henan, China), bis(trichloromethyl)carbonate (GL Biochem Co., Shanghai, China), carboxylic acids, dichloromethane, and triethylamine were commercial reagents (Sinopharm Chemical Reagent Co., Shanghai, China). Target compounds (II-1–II-n) were synthesized by the acylations of I with corresponding carboxylic acid or acyl chloride (7) (Scheme 1; Table 1).

Method A. General Synthetic Procedures for II-1–II-19. With nitrogen protection, to a solution of I (0.174 g, 1 mmol) in dichloromethane (10 mL)

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Table 1. Title Compounds and Inhibition of Spore Germination against *B. cinerea*

					
No.	R	IC ₅₀ , µg/ml (± SD)	No.	R	IC ₅₀ , µg/ml (± SD)
II-1	H ₃ C—	> 500	II-14	H ₃ C—O—  —CH ₂ —	118.08 ± 1.26
II-2	C ₂ H ₅ —	> 500	II-15	 —O—CH ₂ —	303.04 ± 0.90
II-3	C ₃ H ₇ —	> 500	II-16	Cl—  —O—CH ₂ —	108.12 ± 3.46
II-4	CH ₃ (CH ₂) ₂ CH ₂ —	254.27 ± 1.05	II-17		301.63 ± 2.27
II-5	CH ₃ (CH ₂) ₃ CH ₂ —	129.29 ± 0.94	II-18	CH ₂ =CH—	32.16 ± 0.35
II-6	(CH ₃) ₂ CH—	133.99 ± 0.67	II-19	CH ₂ =C(CH ₃)—	64.04 ± 1.36
II-7	(C ₂ H ₅) ₂ CH—	276.60 ± 0.62	II-20		81.94 ± 0.73
II-8	(CH ₃) ₂ CHCH ₂ CH ₂ —	334.60 ± 2.78	II-21	O ₂ N— 	93.32 ± 1.22
II-9	 —CH ₂ —	168.42 ± 0.16	II-22		441.73 ± 1.17
II-10	Cl—  —CH ₂ —	17.27 ± 0.45	II-23	Cl— 	66.85 ± 0.80
II-11	 —CH ₂ —	> 500	II-24		17.17 ± 0.34
II-12	 —CH ₂ —CH ₂ —	125.76 ± 0.72	II-25		103.71 ± 1.84
II-13	 —CH(C ₂ H ₅)—	185.83 ± 0.51	II-26		151.98 ± 1.07
Pyrimethanil		209.46 ± 0.76			

were added triethylamine (0.3 mL, 2.1 mmol) and carboxylic acid (1 mmol). After the mixture had been stirred for 5 min in an ice–water bath, bis(trichloromethyl) carbonate (BTC, 40 mg, 1 mmol) in dichloromethane (2 mL) was added, and the mixture was stirred overnight at room temperature. Saturated NaHCO₃ solution (20 mL) was added to the mixture, and the mixture was extracted by dichloromethane (3 × 15 mL). The organic extracts were combined, washed with water and saturated NaCl solution in that order, dried over Na₂SO₄, and finally concentrated under vacuum. The concentrated mixture was subjected to a silica gel column, and eluted by the mixture of petroleum ether and ethyl acetate (5:1, v/v) to give target compounds.

Method B. General Synthetic Procedures for II-20–II-26. With nitrogen protection, to a solution of **I** (0.174 g, 1 mmol) in dichloromethane (10 mL) was added triethylamine (0.3 mL, 2.1 mmol). Carboxylic chloride (1 mmol) in dichloromethane (2 mL) was added in an ice–water bath, and the mixture was stirred for 5 h at room temperature. After the solvent had been evaporated, saturated NH₄Cl solution (10 mL) was added, and the mixture was extracted by dichloromethane (3 × 15 mL). The organic extracts were combined, washed with water and saturated NaCl solution in that order, dried over

Na₂SO₄, and finally concentrated under vacuum. After purification with a silica gel column as described above, target compounds were obtained.

1-Acetyl-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-1). Yield, 60.1%; mp, 102–104 °C; ¹H NMR (CDCl₃), δ 2.20 (s, 3H, CH₃ of isopropenyl), 2.77 (s, 3H, CH₃ of acetyl), 5.26 (s, 1H, C=CH₂), 5.47 (s, 1H, C=CH₂), 7.06 (d, *J* = 8.0 Hz, 1H, Ph), 7.14–7.27 (m, 2H, Ph), 8.22 (d, *J* = 8.0 Hz, 1H, Ph); ¹³C NMR (CDCl₃), δ 19.8 (CH₃ of isopropenyl), 25.8 (CH₃ of acetyl), 105.6, 115.1, 115.9, 122.9, 124.6, 126.4, 129.3, 137.0, 150.8 (CO), 170.6 (CO of acetyl). Anal. Calcd for C₁₂H₁₂N₂O₂: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.82; H, 5.65; N, 12.82.

1-(Prop-1-en-2-yl)-3-propionyl-1H-benzo[d]imidazol-2(3H)-one (II-2). Yield, 65.8%; mp, 126–128 °C; ¹H NMR (CDCl₃), δ 1.26 (t, *J* = 7.5 Hz, 3H, CH₃ of propionyl), 2.19 (s, 3H, CH₃ of isopropenyl), 3.19 (q, *J* = 7.5 Hz, 2H, CH₂ of propionyl), 5.25 (s, 1H, C=CH₂), 5.47 (s, 1H, C=CH₂), 7.06 (d, *J* = 8.0 Hz, 1H, Ph), 7.14–7.27 (m, 2H, Ph), 8.24 (d, *J* = 8.0 Hz, 1H, Ph); ¹³C NMR (CDCl₃), δ 8.2 (CH₃ of propionyl), 19.8 (CH₃ of isopropenyl), 31.0 (CH₂ of propionyl), 108.6, 115.4, 115.9, 122.9, 124.4, 126.6, 129.4, 137.1, 150.7 (CO), 174.6 (CO of propionyl). Anal. Calcd for C₁₃H₁₄N₂O₂: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.96; H, 6.19; N, 12.09.

1-Butyryl-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-3). Yield, 90.0%; mp, 104–106 °C; ^1H NMR (CDCl_3), δ 1.05 (t, J = 7.5 Hz, 3H, CH_3 of butyryl), 1.81 (m, 2H, CH_2 of butyryl), 2.19 (s, 3H, CH_3 of isopropenyl), 3.15 (t, J = 7.5 Hz, 2H, CH_2 of butyryl), 5.25 (s, 1H, $\text{C}=\text{CH}_2$), 5.47 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.16–7.27 (m, 2H, Ph), 8.24 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 13.7 (CH_3 of butyryl), 17.6 (CH_2 of butyryl), 19.8 (CH_3 of isopropenyl), 39.3 (CH_2 of butyryl), 108.6, 115.4, 115.9, 122.9, 124.4, 126.6, 129.4, 137.1, 150.7 (CO), 173.7 (CO of butyryl). Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.92; H, 6.65; N, 11.37.

1-Pentanoyl-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-4). Yield, 88.4%; mp, 114–116 °C; ^1H NMR (CDCl_3), δ 0.97 (t, J = 7.8 Hz, 3H, CH_3 of pentanoyl), 1.42–1.46 (m, 2H, CH_2 of pentanoyl), 1.76 (m, 2H, CH_2 of pentanoyl), 2.19 (s, 3H, CH_3), 3.11 (t, J = 7.4 Hz, 2H, CH_2 of pentanoyl), 5.26 (s, 1H, $\text{C}=\text{CH}_2$), 5.47 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.14–7.27 (m, 2H, Ph), 8.24 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 13.9 (CH_3 of pentanoyl), 19.8, 22.3 (CH_2 of pentanoyl), 26.2 (CH_2 of pentanoyl), 37.2 (CH_2 of pentanoyl), 108.6, 115.4, 115.9, 122.9, 124.4, 126.6, 129.4, 137.0, 150.7 (CO), 174.0 (CO of pentanoyl). Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.95; H, 7.24; N, 10.65.

1-Hexanoyl-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-5). Yield, 90.1%; mp, 42–44 °C; ^1H NMR (CDCl_3), δ 0.92 (t, J = 7.8 Hz, 3H, CH_3 of hexanoyl), 1.36–1.43 (m, 4H, 2 $\times$ CH_2 of hexanoyl), 1.78 (t, J = 7.8 Hz, 2H, CH_2 of hexanoyl), 2.19 (s, 3H, CH_3), 3.16 (t, J = 7.8 Hz, 2H, CH_2 of hexanoyl), 5.27 (s, 1H, $\text{C}=\text{CH}_2$), 5.47 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.14–7.23 (m, 2H, Ph), 8.24 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 13.9 (CH_3 of hexanoyl), 19.8, 22.5 (CH_2 of hexanoyl), 23.8 (CH_2 of hexanoyl), 31.3 (CH_2 of hexanoyl), 37.4 (CH_2 of hexanoyl), 108.6, 115.4, 115.9, 122.9, 124.4, 126.6, 129.4, 137.1, 150.7 (CO), 173.9 (CO of hexanoyl). Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.68; H, 7.52; N, 10.15.

1-Isobutyryl-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-6). Yield, 89.7%; mp, 88–90 °C; ^1H NMR (CDCl_3), δ 1.26 (d, J = 7.4 Hz, 3H, CH_3 of isobutyryl), 1.30 (d, J = 7.4 Hz, 3H, CH_3 of isobutyryl), 2.22 (s, 3H, CH_3 of isopropenyl), 4.02–4.06 (m, 1H, CH of isobutyryl), 5.26 (s, 1H, $\text{C}=\text{CH}_2$), 5.47 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.14–7.27 (m, 2H, Ph), 8.23 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 18.9 (2 $\times$ CH_3 of isobutyryl), 19.8 (CH_3 of isopropenyl), 34.3 (CH of isobutyryl), 108.6, 115.4, 116.1, 122.9, 124.4, 126.9, 129.5, 137.1, 150.4 (CO), 178.3 (CO of isobutyryl). Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.95; H, 6.65; N, 11.35.

1-(2-Ethylbutanoyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-7). Yield, 91.0%; mp, 118–120 °C; ^1H NMR (CDCl_3), δ 0.97 (t, J = 7.0 Hz, 6H, 2 $\times$ CH_3 of 2-ethylbutanoyl), 1.66 (m, 4H, 2 $\times$ CH_2 of 2-ethylbutanoyl), 2.20 (s, 3H, CH_3), 2.30–2.32 (m, 1H, CH of 2-ethylbutanoyl), 5.27 (s, 1H, $\text{C}=\text{CH}_2$), 5.48 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.16–7.26 (m, 2H, Ph), 8.26 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 11.6 (2 $\times$ CH_3 of 2-ethylbutanoyl), 19.7, 24.3 (2 $\times$ CH_2 of 2-ethylbutanoyl), 47.4 (CH of 2-ethylbutanoyl), 105.8, 114.9, 114.7, 122.6, 124.2, 126.0, 129.3, 137.1, 151.0 (CO), 170.4 (CO of 2-ethylbutanoyl). Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.72; H, 7.48; N, 10.15.

1-(4-Methylpentanoyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-8). Yield, 81.1%; mp, 70–72 °C; ^1H NMR (CDCl_3), δ 0.96 (d, J = 7.6 Hz, 6H, 2 $\times$ CH_3 of 4-methylpentanoyl), 1.66–1.69 (m, 2H, CH_2 of 4-methylpentanoyl), 1.66–1.69 (m, 1H, CH of 4-methylpentanoyl), 2.20 (s, 3H, CH_3), 3.18 (t, J = 7.6, 2H, CH_2 of 4-methylpentanoyl), 5.26 (s, 1H, $\text{C}=\text{CH}_2$), 5.47 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.16–7.26 (m, 2H, Ph), 8.23 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 22.4 (2 $\times$ CH_3 of 4-methylpentanoyl), 27.7 (CH_2 of 4-methylpentanoyl), 32.9 (CH of 4-methylpentanoyl), 35.5 (CH_2 of 4-methylpentanoyl), 108.6, 115.5, 115.9, 122.9, 124.4, 126.6, 129.4, 137.1, 150.7 (CO), 174.2 (CO of 4-methylpentanoyl). Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.75; H, 7.49; N, 10.12.

1-(2-Phenylacetyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-9). Yield, 59.2%; mp, 124–126 °C; ^1H NMR (CDCl_3), δ 2.20 (s, 3H, CH_3), 4.54 (s, 2H, CH_2 of 2-phenylacetyl), 5.27 (s, 1H, $\text{C}=\text{CH}_2$), 5.49 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.12–7.38 (m, 7H, Ph), 8.21 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 43.5 (CH_2 of

2-phenylacetyl), 108.6, 115.7, 116.0, 123.0, 124.7, 126.5, 127.1, 128.5, 129.4, 129.9, 133.5, 136.9, 150.4 (CO), 171.7 (CO of 2-phenylacetyl). Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 74.12; H, 5.60; N, 9.46.

1-(2-(4-Chlorophenyl)acetyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-10). Yield, 73.6%; mp, 90–92 °C; ^1H NMR (CDCl_3), δ 2.20 (s, 3H, CH_3), 4.51 (s, 2H, CH_2 of (4-chlorophenyl)acetyl), 5.27 (s, 1H, $\text{C}=\text{CH}_2$), 5.49 (s, 1H, $\text{C}=\text{CH}_2$), 7.06 (d, J = 8.0 Hz, 1H, Ph), 7.12–7.38 (m, 6H, Ph), 8.20 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 42.8 (CH_2 of (4-chlorophenyl)acetyl), 108.7, 115.7, 116.0, 123.1, 124.8, 126.5, 128.7, 129.5, 131.3, 132.0, 133.1, 136.9, 150.6 (CO), 171.2 (CO of (4-chlorophenyl)acetyl). Anal. Calcd for $\text{C}_{18}\text{H}_{15}\text{N}_2\text{O}_2\text{Cl}$: C, 66.16; H, 4.63; N, 8.57. Found: C, 66.38; H, 4.69; N, 8.45.

1-(2-(Naphthalen-2-yl)acetyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-11). Yield, 72.5%; mp, 128–130 °C; ^1H NMR (CDCl_3), δ 2.25 (s, 3H, CH_3), 4.99 (s, 2H, CH_2 of 2-(naphthalen-2-yl)acetyl), 5.32 (s, 1H, $\text{C}=\text{CH}_2$), 5.51 (s, 1H, $\text{C}=\text{CH}_2$), 7.08–7.14 (m, 2H, Ph), 7.20–7.25 (m, 1H, Ph), 7.46–7.53 (m, 4H, Ph), 7.83–7.94 (m, 4H, Ph), 8.16 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.9, 41.4 (CH_2 of 2-(naphthalen-2-yl)acetyl), 108.7, 115.7, 116.1, 123.0, 123.9, 124.7, 125.4, 125.7, 126.3, 126.6, 128.2, 128.3, 128.8, 129.5, 130.3, 132.4, 133.8, 137.0, 150.9 (CO), 171.4 (CO of 2-(naphthalen-2-yl)acetyl). Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.35; H, 5.39; N, 8.09.

1-(3-Phenylpropanoyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-12). Yield, 51.2%; mp, 78–80 °C; ^1H NMR (CDCl_3), δ 2.18 (s, 3H, CH_3), 3.11 (t, J = 7.0 Hz, 2H, CH_2 of 2-phenylacetyl), 3.50 (t, J = 7.0 Hz, 2H, CH_2 of 2-phenylacetyl), 5.24 (s, 1H, $\text{C}=\text{CH}_2$), 5.46 (s, 1H, $\text{C}=\text{CH}_2$), 7.05 (d, J = 8.0 Hz, 1H, Ph), 7.14–7.27 (m, 7H, Ph), 8.24 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 30.1 (CH_2 of 2-phenylacetyl), 39.0 (CH_2 of 2-phenylacetyl), 108.6, 115.4, 115.9, 122.9, 124.6, 126.1, 126.5, 128.4, 128.6, 129.4, 137.0, 140.6, 150.4 (CO), 172.9 (CO of 2-phenylacetyl). Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.65; H, 6.03; N, 8.95.

1-(2-Phenylbutanoyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-13). Yield, 65.1%; mp, 48–50 °C; ^1H NMR (CDCl_3), δ 0.92 (t, J = 7.8 Hz, 3H, CH_3 of 2-phenylbutanoyl), 1.91, 2.26 (m, 2H, CH_2 of 2-phenylbutanoyl), 2.14 (s, 3H, CH_3), 5.20 (s, 1H, $\text{C}=\text{CH}_2$), 5.44 (s, 1H, $\text{C}=\text{CH}_2$), 5.26 (m, 1H, CH of 2-phenylbutanoyl), 6.99 (d, J = 7.0 Hz, 1H, Ph), 7.10–7.33 (m, 5H, Ph), 7.48 (d, J = 7.0, 2H, Ph), 8.25 (d, J = 8.0, 1H, Ph); ^{13}C NMR (CDCl_3), δ 12.1 (CH_3 of 2-phenylbutanoyl), 19.7, 27.4 (CH_2 of 2-phenylbutanoyl), 52.0 (CH of 2-phenylbutanoyl), 108.4, 115.6, 116.0, 122.8, 124.5, 126.8, 127.1, 128.4, 128.8, 129.3, 136.9, 138.5, 150.3 (CO), 174.5 (CO of 2-phenylbutanoyl). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 75.16; H, 6.38; N, 8.46.

1-(2-(4-Methoxyphenyl)acetyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-14). Yield, 80.1%; mp, 118–120 °C; ^1H NMR (CDCl_3), δ 2.20 (s, 3H, CH_3), 3.80 (s, 3H, CH_3 of 2-(4-methoxyphenyl)acetyl), 4.48 (s, 2H, CH_2 of 2-(4-methoxyphenyl)acetyl), 5.26 (s, 1H, $\text{C}=\text{CH}_2$), 5.48 (s, 1H, $\text{C}=\text{CH}_2$), 6.89 (d, J = 7.8 Hz, 2H, Ph), 7.05 (d, J = 8.0 Hz, 1H, Ph), 7.14–7.22 (m, 2H, Ph), 7.30 (d, J = 7.8 Hz, 2H, Ph), 8.21 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 42.6 (CH_2 of 2-(4-methoxyphenyl)acetyl), 55.2 (CH_3 of 2-(4-methoxyphenyl)acetyl), 108.6, 113.9, 115.6, 116.0, 122.9, 124.6, 125.6, 126.7, 129.5, 130.9, 137.0, 150.7 (CO), 158.7, 172.1 (CONH). Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.93; H, 5.72; N, 8.50.

1-(2-Phenoxyacetyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-15). Yield, 46.4%; mp, 118–120 °C; ^1H NMR (CDCl_3), δ 2.22 (s, 3H, CH_3), 5.29 (s, 1H, $\text{C}=\text{CH}_2$), 5.50 (s, 1H, $\text{C}=\text{CH}_2$), 5.43 (s, 2H, CH_2 of 2-phenoxyacetyl), 6.99–7.03 (m, 4H, Ph), 7.17–7.32 (m, 4H, Ph), 8.25 (d, J = 7.8 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 68.3 (CH_2 of 2-phenoxyacetyl), 108.9, 114.8, 115.6, 115.8, 121.6, 123.3, 125.1, 125.9, 129.5, 130.0, 136.8, 150.6 (CO), 157.9, 168.6 (CO of 2-phenoxyacetyl). Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.34; H, 5.30; N, 8.89.

1-(2-(4-Chlorophenoxy)acetyl)-3-(prop-1-en-2-yl)-1H-benzod[*l*]imidazol-2(3H)-one (II-16). Yield, 77.5%; mp, 136–138 °C; ^1H NMR (CDCl_3), δ 2.22 (s, 3H, CH_3), 5.29 (s, 1H, $\text{C}=\text{CH}_2$), 5.50 (s, 1H, $\text{C}=\text{CH}_2$), 5.40 (s, 2H, CH_2 of 2-(4-chlorophenoxy)acetyl), 6.93–6.96 (m, 2H, Ph), 7.09 (d, J = 8.0 Hz, 1H, Ph), 7.19–7.27 (m, 4H, Ph), 8.23 (d, J = 8.0 Hz, 1H, Ph); ^{13}C NMR (CDCl_3), δ 19.8, 68.5 (CH_2 of 2-(4-chlorophenoxy)acetyl), 109.0,

115.8, 116.1, 123.4, 124.6, 125.2, 125.6, 126.6, 129.4, 130.0, 136.7, 150.5 (CO), 156.4, 168.2 (CO of 2-(4-chlorophenoxy)acetyl). Anal. Calcd for $C_{18}H_{15}ClN_2O_3$: C, 63.07; H, 4.41; N, 8.17. Found: C, 63.22; H, 4.49; N, 8.00.

1-(4-(1H-Indol-3-yl)butanoyl)-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-17). Yield, 65.4%; mp, 176–178 °C; 1H NMR ($CDCl_3$), δ 2.18 (s, 3H, CH_3), 2.22 (m, 2H, CH_2 of 4-(indol-3-yl)butanoyl), 2.92 (m, 2H, CH_2 of 4-(indol-3-yl)butanoyl), 3.27 (m, 2H, CH_2 of 4-(indol-3-yl)butanoyl), 5.24 (s, 1H, $C=CH_2$), 5.46 (s, 1H, $C=CH_2$), 7.03–7.22 (m, 5H, Ph or heterocycle), 7.25 (s, 1H, heterocycle), 7.33 (d, $J = 7.5$ Hz, 1H, Ph), 7.65 (d, $J = 7.5$ Hz, 1H, Ph), 7.99 (s, 1H, NH), 8.23 (d, $J = 8.0$ Hz, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.8, 24.4 (CH_2 of 4-(indol-3-yl)butanoyl), 24.5 (CH_2 of 4-(indol-3-yl)butanoyl), 37.2 (CH_2 of 4-(indol-3-yl)butanoyl), 108.5, 111.0, 115.5, 115.7, 115.9, 118.9, 119.1, 121.5, 121.8, 122.8, 124.4, 126.6, 127.4, 129.4, 136.3, 137.0, 150.1 (CO), 173.4 (CO of 4-(indol-3-yl)butanoyl). Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.69; H, 5.98; N, 11.52.

1-Acryloyl-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-18). Yield, 77.1%; mp, 108–110 °C; 1H NMR ($CDCl_3$), δ 2.20 (s, 3H, CH_3 of isopropenyl), 5.27 (s, 1H, $C=CH_2$), 5.48 (s, 1H, $C=CH_2$), 5.99 (d, $J = 16.2$ Hz, 1H, CH_2 of acryloyl), 6.68 (d, $J = 12.8$ Hz, 1H, CH_2 of acryloyl), 7.06 (d, $J = 8.0$ Hz, 1H, Ph), 7.15–7.27 (m, 2H, Ph), 7.74 (dd, $J = 16.2$, 12.8 Hz, 1H, CH of acryloyl), 8.23 (d, $J = 8.0$ Hz, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.8, 108.7, 115.5, 116.5, 123.0, 124.7, 126.6, 129.1 (CH_2 of acryloyl), 129.7, 132.1 (CH of acryloyl), 137.0, 150.7 (CO), 165.3 (CO of acryloyl). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.60; H, 5.36; N, 12.15.

1-Methacryloyl-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-19). Yield, 45.2%; mp, 124–126 °C; 1H NMR ($CDCl_3$), δ 2.17 (s, 3H, CH_3 of methacryloyl), 2.21 (s, 3H, CH_3), 5.25 (s, 1H, $C=CH_2$), 5.44 (s, 1H, $C=CH_2$), 5.41, 5.61 (s, 2H, CH_2 of methacryloyl), 7.08 (d, $J = 8.0$ Hz, 1H, Ph), 7.14–7.26 (m, 2H, Ph), 7.98 (d, $J = 8.0$ Hz, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.7, 20.1 (CH_3 of methacryloyl), 108.9, 110.0 (CH_2 of methacryloyl), 114.8, 114.9, 122.8, 124.4, 126.6, 129.6, 137.5, 140.5 (C of methacryloyl), 154.8 (CO), 170.3 (CO of methacryloyl). Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.72; H, 5.95; N, 11.26.

1-Benzoyl-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-20). Yield, 86.3%; mp, 118–120 °C; 1H NMR ($CDCl_3$), δ 2.16 (s, 3H, CH_3), 5.26 (s, 1H, $C=CH_2$), 5.42 (s, 1H, $C=CH_2$), 7.12 (d, $J = 8.4$ Hz, 1H, Ph), 7.18–7.26 (m, 2H, Ph), 7.49 (t, $J = 7.4$, 2H, Ph), 7.60 (t, $J = 7.4$ Hz, 1H, Ph), 7.80 (d, $J = 7.4$ Hz, 2H, Ph), 7.97 (d, $J = 8.4$, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.7, 109.0, 114.7, 114.9, 122.8, 124.5, 127.0, 128.0, 129.3, 129.9, 132.8, 133.6, 137.1, 150.2 (CO), 168.5 (CO of benzoyl). Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.56; H, 5.18; N, 9.86.

1-(4-Nitrobenzoyl)-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-21). Yield, 46.1%; mp, 142–144 °C; 1H NMR ($CDCl_3$), δ 2.14 (s, 3H, CH_3), 5.26 (s, 1H, $C=CH_2$), 5.44 (s, 1H, $C=CH_2$), 7.14 (d, $J = 7.8$ Hz, 1H, Ph), 7.23–7.30 (m, 2H, Ph), 7.88 (d, $J = 9.0$ Hz, 2H, Ph), 8.10 (d, $J = 7.8$ Hz, 1H, Ph), 8.20 (d, $J = 9.0$ Hz, 2H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.7, 109.3, 115.2, 115.3, 123.2, 123.3, 125.3, 126.3, 129.7, 130.0, 136.8, 139.7, 149.6, 150.0 (CO), 167.1 (CO of 4-nitrobenzoyl). Anal. Calcd for $C_{17}H_{13}N_3O_4$: C, 63.16; H, 4.05; N, 13.00. Found: C, 63.42; H, 4.15; N, 12.80.

1-(2-Nitrobenzoyl)-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-22). Yield, 90.1%; mp, 146–148 °C; 1H NMR ($CDCl_3$), δ 2.07 (s, 3H, CH_3), 5.21 (s, 1H, $C=CH_2$), 5.39 (s, 1H, $C=CH_2$), 7.06 (d, $J = 8.0$ Hz, 1H, Ph), 7.24–7.31 (m, 2H, Ph), 7.52 (d, $J = 8.2$ Hz, 1H, Ph), 7.66 (t, $J = 8.2$, 1H, Ph), 7.80 (t, $J = 8.2$, 1H, Ph), 8.25 (d, $J = 8.0$ Hz, 1H, Ph), 8.37 (d, $J = 8.2$, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.6, 109.0, 115.5, 115.7, 123.3, 124.1, 125.2, 126.1, 127.8, 129.8, 130.4, 132.3, 134.6, 136.6, 145.0, 150.0 (CO), 165.6 (CO of 2-nitrobenzoyl). Anal. Calcd for $C_{17}H_{13}N_3O_4$: C, 63.16; H, 4.05; N, 13.00. Found: C, 63.32; H, 4.18; N, 12.75.

1-(4-Chlorobenzoyl)-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-23). Yield, 65.0%; mp, 138–140 °C; 1H NMR ($CDCl_3$), δ 2.16 (s, 3H, CH_3), 5.26 (s, 1H, $C=CH_2$), 5.43 (s, 1H, $C=CH_2$), 7.12 (d, $J = 7.8$ Hz, 1H, Ph), 7.19–7.26 (m, 2H, Ph), 7.45 (d, $J = 8.0$, 2H, Ph), 7.74 (d, $J = 8.0$ Hz, 2H, Ph), 7.96 (d, $J = 7.8$ Hz, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.7, 109.1, 114.8, 115.0, 122.9, 124.7, 126.8, 128.9, 129.9, 130.8, 131.9, 137.1, 139.1,

150.3 (CO), 167.9 (CO of 4-chlorobenzoyl). Anal. Calcd for $C_{17}H_{13}N_2O_2Cl$: C, 65.29; H, 4.19; N, 8.96. Found: C, 65.45; H, 4.25; N, 8.75.

1-(2-Chlorobenzoyl)-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-24). Yield, 96.4%; mp, 82–86 °C; 1H NMR ($CDCl_3$), δ 2.12 (s, 3H, CH_3), 5.23 (s, 1H, $C=CH_2$), 5.39 (s, 1H, $C=CH_2$), 7.09 (d, $J = 7.8$ Hz, 1H, Ph), 7.21–7.47 (m, 6H, Ph), 8.27 (d, $J = 7.8$ Hz, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.6, 108.9, 115.0, 115.5, 123.1, 124.8, 126.1, 126.7, 128.1, 129.2, 129.9, 130.7, 131.5, 135.1, 136.8, 149.6 (CO), 166.3 (CO of 2-chlorobenzoyl). Anal. Calcd for $C_{17}H_{13}N_2O_2Cl$: C, 65.29; H, 4.19; N, 8.96. Found: C, 65.40; H, 4.29; N, 8.78.

1-(Furan-2-carbonyl)-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-25). Yield, 64.2%; mp, 104–106 °C; 1H NMR ($CDCl_3$), δ 2.19 (s, 3H, CH_3), 5.29 (s, 1H, $C=CH_2$), 5.46 (s, 1H, $C=CH_2$), 6.61 (dd, $J = 3.6$, 1.2 Hz, 1H, CH of furan-2-carbonyl), 7.09 (d, $J = 7.8$ Hz, 1H, Ph), 7.16–7.26 (m, 2H, Ph), 7.54 (d, $J = 3.6$ Hz, 1H, CH of furan-2-carbonyl), 7.70 (d, $J = 1.2$ Hz, 1H, CH of furan-2-carbonyl), 7.84 (d, $J = 7.8$, 1H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.8, 109.0, 112.3 (CH of furan-2-carbonyl), 114.3, 115.1, 121.6 (CH of furan-2-carbonyl), 122.7, 124.3, 126.9, 129.8, 137.2, 146.1 (CH of furan-2-carbonyl), 147.4 (C of furan-2-carbonyl), 149.9 (CO), 157.0 (CO of furan-2-carbonyl). Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.42; H, 4.62; N, 10.26.

1-Isonicotinoyl-3-(prop-1-en-2-yl)-1H-benzo[d]imidazol-2(3H)-one (II-26). Yield, 81.0%; mp, 132–134 °C; 1H NMR ($CDCl_3$), δ 2.15 (s, 3H, CH_3), 5.26 (s, 1H, $C=CH_2$), 5.44 (s, 1H, $C=CH_2$), 7.12 (d, $J = 8.4$ Hz, 1H, Ph), 7.22–7.30 (m, 2H, Ph), 7.55 (d, $J = 7.8$, 2H, Ph), 8.10 (d, $J = 8.4$ Hz, 1H, Ph), 8.79 (d, $J = 7.8$, 2H, Ph); ^{13}C NMR ($CDCl_3$), δ 19.7, 109.2, 115.3, 115.4, 121.9, 123.2, 125.2, 126.3, 130.0, 136.8, 141.5, 150.0 (CO), 167.2 (CO of isonicotinoyl). Anal. Calcd for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 69.03; H, 4.75; N, 14.86.

Microorganism and Preparation of Spore Suspension. The tested fungal pathogen, *B. cinerea*, was provided by the Institute of Plant Disease, Northwest A&F University. The strain was retrieved from the storage tube and cultured for 2 weeks at 20 °C on potato dextrose agar (PDA, Difco). Plates were then flooded with sterile distilled water, and conidia were scraped with a glass stick. Mycelial debris was removed by filtration through double-layer cheesecloth, and the spores were harvested and suspended in sterile distilled water containing 0.1% (v/v) Tween 20. Spores were counted using a hemocytometer and adjusted to 1.0×10^6 spores/mL (16).

Spore Germination Assay. The tested samples (10 mg) dissolved in methanol (0.1 mL) were diluted with sterile distilled water to prepare 10 mL stock solution, which was further diluted to prepare test solutions in which the final concentration of methanol was <1% (v/v). A series of concentrations of tested samples and one control (1% methanol with sterile distilled water) were separately tested for spore germination of *B. cinerea*. The samples were inoculated with spore suspension of *B. cinerea* containing 1.0×10^6 spores/mL. Aliquots of 10 μ L of prepared spore suspension were placed on separate glass slides in triplicate. Slides containing the spores were incubated in a moisture chamber at 25 °C for 6 h. Each slide was then observed under the microscope for spore germination. The spore-generated germ tubes were enumerated, and percentage of spore germination was calculated. Pyrimethanil was preferred as the positive control.

Statistical Analysis. The experimental data of the fungicidal activities were analyzed using SPSS 13.0 for Windows.

RESULTS AND DISCUSSION

Synthesis. *N*-Acyl derivatives of isopropenyl benzimidazolone could be readily synthesized by the acylation of **I** with corresponding carboxylic acid or acyl chloride in good yields. **II-1** had been reported to be synthesized using the same procedure (13), and it could also be prepared from 4-methyl-2,3-dihydro-1*H*-1,5-benzodiazepin-2-one by acetylation in pyridine (17). In a program of screening antitumor compounds, **II-20** was once obtained by reaction of benzoyl chloride with **I** (7), but the fungicidal activity of these two compounds was not mentioned in the references.

The title compounds, including **II-1** and **II-20**, were characterized with 1H NMR, ^{13}C NMR, and elemental analysis.

Fungicidal Activity. The fungicidal activities of the title compounds against *B. cinerea* were evaluated by spore germination assay, and the results are listed in Table 1. The fungicidal activity was strongly influenced by the acyl group on the nitrogen atom. Among the saturated aliphatic acid derivatives (II-1–II-5), the activities became higher with extension of the carbon chain. When a side chain was introduced to the main carbon chain, a methyl or an ethyl at the α -position (II-6 and II-7) helped with their activities, because their activities were much higher than those of II-2 and II-3. However, compound II-8, with a methyl group at the γ -position of pentanoyl, gave a little lower activity than corresponding compound II-4. Similarly, II-17, with a bulky indole ring at the γ -position of butanoyl, also exhibited lower activity.

The introduction of a hydrophobic benzene ring to the alkyl chain increased the fungicidal activities to a large extent. Phenyl-ethylcarbonyl derivative II-12 and benzylcarbonyl derivatives (II-9, II-10, and II-13) showed much higher activities than corresponding alkyl derivatives II-1–II-3. Among them, 4-chlorobenzylcarbonyl compound II-10 exhibited uncommon activity, with a median inhibitory concentration (IC_{50}) value of 17.27 μ g/mL. Phenoxyacetyl compound II-15 and 4-chlorophenoxyacetyl compound II-16 also gave moderate activities with II-16 higher than II-15, which also indicates that a chloro atom at the para-position of the benzene ring could increase the activity. Compound II-11, bearing a bulky phenanthryl, gave very low activity.

Compared to most of the alkyl acyl derivatives and control compound pyrimethanil, acrylamide compounds II-18 and II-19 showed higher activities, as their median inhibitory concentration (IC_{50}) values were only 32.42 and 63.45 μ g/mL, respectively. This implied that α,β -unsaturated carbonyl might play an important role in their fungicidal activity.

Substituted benzoyl (II-20, II-21, II-23, and II-24) and other aromatic carbonyl derivatives (II-25 and II-26) of isopropenyl benzimidazolone also exhibited stronger inhibiting activity than alkyl acyl derivatives and pyrimethanil. The type and position of the substituted group introduced to the benzene ring could obviously affect the bioactivity. When chloro was introduced to the ortho- or para-position of benzoyl, their activities were much higher than corresponding nitro derivatives. Of all the compounds, II-24 exhibited the highest inhibiting activity, with $IC_{50} = 17.17 \mu$ g/mL.

In conclusion, 1-acyl-3-isopropenylbenzimidazolone derivatives were prepared and their fungicidal activities against *B. cinerea* evaluated. Although some derivatives of acrylamide, phenylacetamide, and benzamides exhibited good fungicidal activity, there is no obvious structure–activity relationship tendency in general. Indeed, the experiment mentioned above is only a preliminary investigation, and there are more works to be carried out. Nevertheless, because the core skeleton of benzimidazolone possesses great potential in structure modification, it deserves further investigation. The progress will be reported in the future.

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