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# Synthesis and Herbicidal Evaluation of Novel 3-[(α-Hydroxy-substituted)benzylidene]pyrrolidine-2,4-diones

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A series of 3-[(α-hydroxy-substituted) benzylidene]pyrrolidine-2,4-dione derivatives were synthesized as candidate herbicides by reacting different aroyl acetates with *N*-substituted glycine esters. The new compounds were identified by $^1$H NMR spectroscopy and elemental analyses. Their herbicidal activities were evaluated. Some compounds exhibited excellent herbicidal activities at a dose of 187.5 g/ha. A suitable electron-donating substituent at the 2- and/or 4-position of the phenyl ring was essential for high herbicidal activity, a result that has not been reported before. It was also found that the title compound's structure−activity relationships were different from those of other similar kinds of earlier compounds, a result that may depend on the enol structure difference.

**KEYWORDS: Herbicide; aroyl acetate; HPPD; electron-donating group; structure−activity relationship (SAR)**

## INTRODUCTION

The inhibitors of 4-hydroxyphenylpyruvate dioxygenase (HPPD, EC 1.13.11.27) constitute a new kind of herbicide (*1*). Generally, potent herbicides of this kind must possess the following structural features: (1) a di- or tricarbonyl methane structure, with one of the carbonyl groups being a substituted benzoyl group; (2) the compound must be able to enolize so that the enolate is capable of inhibiting the HPPD enzyme by competitive combination with $Fe^{2+}$—the reaction center of the HPPD enzyme; (3) electron-withdrawing groups are preferred at both the 2- and 4-positions of the phenyl ring (*2*−*4*). In our previous work (*5*, 6), the natural product **A** (**Figure 1**), which was inhibitory toward HPPD with an $IC_{50} = 18\ \mu M$ (*7*), was modified to **B** (**Figure 1**) by the replacement of acetyl with substituted benzoyl, and the bioassay results showed that when $R^1$ was electron-donating, compound **B** possessed higher herbicidal activities and made the monocotyledonous plants *Echinochloa crus-galli* and *Digitaria sanguinalis* bleached. The analysis of their crystals confirmed that their molecular structures adopted the enol form **B1** (**Figure 1**) and their molecular skeletons contained one enol hydrogen-bonded moiety, formed from benzoyl C═O isomerization (*8*, *9*). On the basis of the action mode of the HPPD inhibitors, the above phenomena revealed that an electron-donating group may not only be favorable to the formation of the enol tautomer **B1** but also reinforce its combination with $Fe^{2+}$—the reaction center of HPPD—through raising the enol-oxygen's electron density. In the meantime, it was also found that when $R^1$ at the phenyl ring was electron-donating and $R^2$ at the nitrogen atom was isopropyl, *tert*-butyl, or methyl, respectively, the *N*-isopropyl compound's herbicidal activity was the highest. To further amplify the structure−activity relationship (SAR) between $R^1$ of **B1** and the resulting activity and to find valuable lead compounds with high herbicidal activity, subsequent optimization of **B1** was focused on varying the electron-donating capability of the substituent $R^1$ while retaining the pyrrolidin-2,4-dione heterocycle. In this paper, we described the synthesis and herbicidal activities of some 3-[(α-hydroxy-substituted)-benzylidene]pyrrolidine-2,4-dione derivatives.

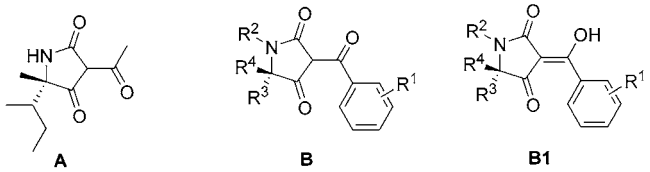


**Figure 1.** Chemical structures of **A**, **B**, and **B1**.

## MATERIALS AND METHODS

**Synthetic Procedures.** Proton NMR spectra were obtained at 300 MHz using a Bruker AC-P300 spectrometer in $CDCl_3$ solution with TMS as internal standard. Chemical shift values ($\delta$) were given in parts per million. Elemental analyses were determined on a Yanaca CHN Corder MT-3 elemental analyzer. Melting points were taken on a Thomas-Hoover melting-point apparatus and were uncorrected. Yields were not optimized.

**General Synthetic Procedure for D1−15 and E1−3.** Solvents were dried according to standard methods and distilled prior to use. Compounds **D1−15** were synthesized as the literature described (*5*, *6*). Compounds **E1−3** were synthesized as the literature described (*5*, *6*, *10*). All of them were identified by $^1$H NMR spectroscopy. The yields of compounds **D1−15** are listed in **Table 1**.

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**Table 1.** Yields of Compounds **D1**–**19**

| compd | appearance | yield (%) | compd | appearance | yield (%) |
|---|---|---|---|---|---|
| **D1** | orange liquid | 50 | **D11** | orange liquid | 30 |
| **D2** | orange liquid | 58 | **D12** | orange liquid | 43 |
| **D3** | orange liquid | 40 | **D13** | orange liquid | 43 |
| **D4** | orange liquid | 68 | **D14** | white solid | 45 |
| **D5** | orange liquid | 64.9 | **D15** | orange liquid | 66 |
| **D6** | orange liquid | 51 | **D16** | orange liquid | 82 |
| **D7** | orange liquid | 43 | **D17** | orange liquid | 87 |
| **D8** | orange liquid | 40 | **D18** | orange liquid | 89 |
| **D9** | orange liquid | 49 | **D19** | orange liquid | 82 |
| **D10** | orange liquid | 53 | | | |

**General Synthetic Procedure for D16−19 (*11*).** To a mixture of NaH/oil dispersion (0.528 g, 50% NaH by weight, 0.264 g of NaH, 11 mmol), 12 mL of diethyl carbonate, and 15 mL of THF was added dropwise a solution of 10 mmol of substituted acetophenone in THF. The mixture was heated at reflux for 3 h. The reaction mixture was poured into water, the pH was adjusted to 9, and the mixture was extracted with methylene chloride. The solvent was removed, and the residue was purified by flash silica gel chromatography using petroleum ether (60−90 °C) and ethyl acetate as the eluent to yield **D16−19**. All of the compounds were identified by $^1$H NMR spectroscopy. The yields of compounds **D16−19** are listed in **Table 1**.

**General Synthetic Procedure for F1−36 (*5, 6, 12*).** A mixture of **D** (4.11 mmol) and **E** (4.30 mmol) in dry xylene (15 mL) was heated at 125−130 °C with stirring for 20 h. The cooled solution was added to methanolic $CH_3ONa$, prepared from Na metal (0.10 g, 4.35 mmol) and methanol (10 mL) at room temperature with stirring. After the above mixture was stirred at room temperature for 48 h, water (30 mL) was added to the reaction mixture and the organic layer was separated and extracted twice with water. The original water layer and the extracts were combined and acidified to pH 2−3 with 2 N HCl under cooling. The acidic solution was extracted three times with chloroform (30 mL), and the extracts were washed with saturated brine and then dried over $Na_2SO_4$. The solvent was removed under reduced pressure to give crude product **F**, which was purified by flash column chromatography on silica gel, using ethyl acetate−petroleum ether as the eluant to afford the pure target product. The melting points, yields, and elemental analyses of compounds **F1−36** are listed in **Table 2**, and their $^1$H NMR are listed in **Table 3**.

**Bioassays.** For comparative purposes, the herbicidal activities of the title compounds (**F1−36**) and the triketone compound, sulcotrione [2-(2-chloro-4-mesylbenzoyl)cyclohexane-1,3-dione], were evaluated using a previously reported procedure (*13*).

*Treatment.* The emulsions of purified compounds were prepared by dissolving them in 100 μL of *N*,*N*-dimethylformamide with the addition of a little Tween 20 and proper water, and in glasshouse tests, it was sprayed using a laboratory belt sprayer delivering a 750 L/ha spray volume. There were two replicates for each treatment. The mixture of the same amount of water, *N*,*N*-dimethylformamide, and Tween 20 was used as control.

*Inhibition of the Root Growth of Rape (Brassica campestris L).* Rape seeds were soaked in distilled water for 4 h before being placed on a filter paper in a 6-cm Petri plate, to which 2 mL of inhibitor solution had been added in advance. Usually, 15 seeds were used on each plate. The plate was placed in a dark room and allowed to germinate for 65 h at 28 (±1) °C. The lengths of 10 rape roots selected from each plate were measured, and the means were calculated. The percentage inhibition was used to describe the control efficiency of the compounds. The herbicidal activity is summarized in **Table 4**.

*Inhibition of the Seedling Growth of Barnyard Grass (Echinochloa crus-galli L. Beauv).* Ten *E. crus-galli* seeds were placed into a 50 mL cup covered with a layer of glass beads and a piece of filter paper at the bottom, to which 5 mL of inhibitor solution had been added in advance. The cup was placed in a bright room, and the seeds were allowed to germinate for 65 h at 28 (±1) °C. The heights of the above-ground parts of the seedlings in each cup were measured and the means calculated. The percentage inhibition was used to describe the control efficiency of the compounds. The herbicidal activity is summarized in **Table 4**.

**Table 2.** Melting Points, Yields, and Elemental Analysis of Compounds **F1**–**36**

| | | | elemental analysis (%, calcd) | | |
|---|---|---|---|---|---|
| compd | mp (°C) | yield (%) | C | H | N |
| **F1–4** | see ref *6* | | | | |
| **F5** | 146–147 | 59.5 | 66.32 (66.42) | 6.58 (6.62) | 4.92 (4.84) |
| **F6** | 178–179 | 57.8 | 62.75 (62.94) | 6.23 (6.27) | 4.73 (4.59) |
| **F7** | 134–135 | 53 | 70.33 (70.31) | 6.95 (7.01) | 5.21 (5.12) |
| **F8** | 147–149 | 56.6 | 71.06 (71.05) | 7.39 (7.37) | 4.99 (4.77) |
| **F9** | 141–142 | 61.2 | 71.77 (71.73) | 5.59 (5.67) | 6.05 (6.06) |
| **F10** | red liquid | 64.5 | 70.35 (70.31) | 6.93 (7.01) | 5.10 (5.12) |
| **F11** | 97–98 | 45.1 | 61.88 (61.88) | 6.56 (6.63) | 3.96 (4.01) |
| **F12** | orange liquid | 50.0 | 60.22 (60.11) | 5.09 (5.04) | 5.11 (5.01) |
| **F13** | 116–117 | 57.5 | 71.06 (71.05) | 7.31 (7.37) | 4.86 (4.87) |
| **F14** | 106–107 | 43.2 | 72.15 (72.35) | 8.01 (7.99) | 4.49 (4.44) |
| **F15** | 140–141 | 50.2 | 62.90 (62.94) | 6.30 (6.27) | 4.61 (4.59) |
| **F16** | orange liquid | 63.2 | 71.31 (71.20) | 5.72 (5.68) | 4.22 (4.15) |
| **F17** | orange liquid | 59.3 | 61.80 (61.88) | 6.69 (6.63) | 3.92 (4.01) |
| **F18** | orange liquid | 84.8 | 61.88 (61.88) | 6.63 (6.63) | 3.85 (4.01) |
| **F19** | orange liquid | 62.1 | 61.82 (61.88) | 6.66 (6.63) | 4.15 (4.01) |
| **F20–21** | see ref *6* | | | | |
| **F22** | 119–121 | 21 | 70.99 (71.01) | 7.44 (7.37) | 4.82 (4.87) |
| **F23** | >141 decomp | 18 | 71.49 (71.73) | 7.89 (7.69) | 4.61 (4.65) |
| **F24** | 135–136 | 17 | 72.31 (72.35) | 7.88 (7.99) | 4.38 (4.44) |
| **F25** | 174–176 | 8.0 | 63.90 (63.93) | 6.60 (6.63) | 4.41 (4.39) |
| **F26** | 161–163 | 61.6 | 66.89 (66.88) | 6.08 (5.96) | 5.08 (4.88) |
| **F27** | 152–154 | 58.9 | 63.65 (63.36) | 5.69 (5.65) | 4.53 (4.62) |
| **F28** | 84–86 | 70.9 | 70.66 (70.83) | 6.19 (6.32) | 4.98 (5.16) |
| **F29** | 133–135 | 61.0 | 65.91 (65.92) | 5.51 (5.53) | 5.12 (5.13) |
| **F30** | 123–124 | 96.8 | 61.28 (61.25) | 5.76 (5.74) | 4.24 (4.20) |
| **F31** | 112–113 | 57.9 | 71.35 (71.56) | 6.53 (6.71) | 5.01 (4.91) |
| **F32** | 96–97 | 52.7 | 72.89 (72.82) | 7.40 (7.40) | 4.47 (4.47) |
| **F33** | brown liquid | 66.5 | 63.23 (63.36) | 5.59 (5.65) | 4.59 (4.65) |
| **F34** | orange liquid | 63.5 | 71.77 (71.63) | 5.12 (5.11) | 4.15 (4.18) |
| **F35** | orange liquid | 87.5 | 62.35 (62.24) | 6.15 (6.09) | 4.15 (4.09) |
| **F36** | orange liquid | 68.2 | 62.35 (62.24) | 6.15 (6.09) | 4.15 (4.09) |

*Pre-emergence.* Sandy clay (100 g) in a plastic box (11 × 7.5 × 6 cm) was wetted with water. Fifteen sprouting seeds of the weed under test were planted in fine earth (0.6 cm depth) in the glasshouse and sprayed with the test compound solution.

*Postemergence.* Seedlings (one leaf and one stem) of the weed were sprayed with the test compounds at the same rate as used for the pre-emergence test.

For both methods, the fresh weights were determined 15 days later, and the percentage inhibition relative to the controls was calculated. The herbicidal activity is summarized in **Tables 5** and **6**.

## RESULTS AND DISCUSSION

**Preparations.** The synthesis of intermediate β-keto esters **D** using two methods (*5*, *6*, *11*) has been reported (**Schemes 1** and **2**). Compounds **D1−15** were synthesized by treating ethyl acetoacetate with acid chloride followed by decomposition with $NH_3{\cdot}H_2O/NH_4Cl$. Because 2,4-dimethoxybenzoic acid and 2-/3-/4-methoxyethoxymethoxybenzoic acid were not stable under reflux with $SOCl_2$ or reacted with $(COCl)_2$ at room temperature for the preparation of the corresponding benzoyl chloride of **D16−19**, we adopted the reaction of substituted acetophenone with diethyl carbonate in the presence of NaH.

Amino acid esters **E1−3** were prepared conveniently from 2-bromoacetic acid ester and primary amines in dry ether (**Scheme 3**) (*10*). **E1** ($R^2$ = *i*-Pr ): yield, 40%; $n_d^{25}$ = 1.4170. **E2** ($R^2$ = *t*-Bu ): yield, 65.4%; $n_d^{25}$ = 1.4225. **E3** ($R^2$ = cyclopropyl): yield, 87.4%; bp 94−96 °C/0.095 MPa; $^1$H NMR δ 0.14−0.37 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 1.05−1.23 (t, 3H, $^3J_{HH}$ = 7

**Table 3.** $^1$H NMR of Compounds **F1**–**36**

| compd | $\delta$ |
|---|---|
| **F1**–**4** | see ref *6* |
| **F5** | 1.21, 1.29 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 1.40–1.50 (t, 3H, $^3J_{HH}$ = 7 Hz, CH$_2$C$\underline{H}_3$), 3.72 (s, 2H, NC$\underline{H}_2$), 4.08–4.18 (qd, 2H, $^3J_{HH}$ = 7 Hz, C$\underline{H}_2$CH$_3$), 6.91–7.10 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.32–8.42 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph) |
| **F6** | 1.16–1.19 (d, 6H, $^3J_{HH}$ = 7 Hz, CH$_2$C$\underline{H}_3$), 3.66 (s, 2H, NC$\underline{H}_2$), 3.90 (s, 6H, Ar–(OC$\underline{H}_3$)$_2$), 4.35–4.70 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 6.79–6.97, 8.00–8.20 (m, 3H,Ph) |
| **F7** | 1.10–1.27 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 2.31 (s, 6H, Ar(C$\underline{H}_3$)$_2$), 3.64 (s, 2H, NC$\underline{H}_2$), 4.37–4.64 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 7.15 (s, 1H, Ph), 7.70 (s, 2H, Ph) |
| **F8** | 1.16–1.43 (m, 12H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 2.86–3.13 (m, 1H, $^3J_{HH}$ = 7 Hz, ArC$\underline{H}$), 3.74 (s, 2H, NC$\underline{H}_2$), 4.44–4.73 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 7.32–7.47, 8.08–8.30 (m, 4H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F9** | 1.13–1.22 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 1.28 (s, 9H, C(C$\underline{H}_3$)$_3$), 3.65 (s, 2H, NC$\underline{H}_2$), 4.40–4.62 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 7.34–7.49 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph), 8.06–8.17 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F10** | 1.10–1.29 (d, 6H, $^3J_{HH}$ =7 Hz, CH(C$\underline{H}_3$)$_2$), 2.29, 2.35 (s–s, 6H, Ar(C$\underline{H}_3$)$_2$), 3.61 (s, 2H, NC$\underline{H}_2$), 4.35–4.62 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 6.92–7.28, 7.26–7.41 (m, 3H, Ph) |
| **F11** | 1.23–1.31 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 3.74 (s, 2H, NC$\underline{H}_2$), 3.96 (s, 9H, Ar(OC$\underline{H}_3$)), 4.51–4.65 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 7.87 (s, 2H, Ph) |
| **F12** | 1.27–1.29 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 3.71 (s, 2H, NCH$_2$), 4.01 (s, 9H, Ar(OCH$_3$)), 4.50–4.74 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 7.31–7.62 (m, 4H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F13** | 0.91–1.01 (t, 3H, $^3J_{HH}$ = 7 Hz, CH$_2$C$\underline{H}_3$), 1.22–1.27 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 1.60–1.76 (m, 2H, $^3J_{HH}$ = 8 Hz, CH$_2$C$\underline{H}_2$CH$_3$), 2.61–2.70 (t, 2H, $^3J_{HH}$ = 8 Hz, ArC$\underline{H}_2$), 3.710 (s, 2H, NC$\underline{H}_2$), 4.51–4.65 (m, 1H, $^3J_{HH}$ = 7 Hz, NCH), 7.26–7.33 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph), 8.13–8.21 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph) |
| **F14** | 0.85–0.94 (t, 3H, $^3J_{HH}$ = 7 Hz, CH$_2$C$\underline{H}_3$), 1.26, 1.24 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 1.29–1.38 (m, 4H, CH$_2$CH$_2$C$\underline{H}_2$CH$_3$), 1.57–1.72 (m, 2H, CH$_2$C$\underline{H}_2$CH$_2$CH$_3$), 2.63–2.72 (t, 2H, $^3J_{HH}$ = 8 Hz, ArC$\underline{H}_2$), 3.72 (s, 2H, NC$\underline{H}_2$), 4.52–4.64 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 7.23–7.33 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph), 8.14–8.20 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph) |
| **F15** | 1.23, 1.25 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 3.64 (s, 2H, NC$\underline{H}_2$), 3.83, 3.86 (s–s, 6H, Ar(OC$\underline{H}_3$)$_2$), 4.49–4.64 (m, 1H, $^3J_{HH}$ = 7 Hz, NCH), 6.48–6.60 (m, 2H, Ph), 7.48, 7.50 (d, $^3J_{HH}$ = 8 Hz, 1H, Ph) |
| **F16** | 1.07–1.22 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 3.63 (s, 2H, NC$\underline{H}_2$), 4.40–4.57 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 6.93–7.95 (m, 9H, Ph) |
| **F17** | 1.24, 1.26 (d, 6H, $^3J_{HH}$ =7 Hz, CH(C$\underline{H}_3$)$_2$), 3.38 (s, 3H, OC$\underline{H}_3$), 3.50–3.58 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OC$\underline{H}_2$), 3.65 (s, 2H, NC$\underline{H}_2$), 3.77–3.85 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OCH$_2$C$\underline{H}_2$), 4.43–4.69 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 5.53 (s, 2H, ArOC$\underline{H}_2$), 6.91–7.58 (m, 4H, Ph) |
| **F18** | 1.24, 1.26 (d, 6H, $^3J_{HH}$ =7 Hz, CH(C$\underline{H}_3$)$_2$), 3.38 (s, 3H, OC$\underline{H}_3$), 3.52–3.58 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OC$\underline{H}_2$), 3.72 (s, 2H, NC$\underline{H}_2$), 3.80–3.86 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OCH$_2$C$\underline{H}_2$), 4.50–4.65 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 5.35 (s, 2H, ArOC$\underline{H}_2$), 6.93–7.93 (m, 4H, Ph) |
| **F19** | 1.24, 1.26 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 3.38 (s, 3H, OC$\underline{H}_3$), 3.52–3.58 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OC$\underline{H}_2$), 3.72 (s, 2H, NC$\underline{H}_2$), 3.80–3.86 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OCH$_2$C$\underline{H}_2$), 4.50–4.65 (m, 1H, $^3J_{HH}$ = 7 Hz, NC$\underline{H}$), 5.35 (s, 2H, ArOC$\underline{H}_2$), 7.11, 7.14 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.30, 8.33 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F20**–**21** | see ref *6* |
| **F22** | 1.51 (s, 9H, C(C$\underline{H}_3$)$_3$), 2.38 (s, 6H, Ar(C$\underline{H}_3$)$_2$), 3.82 (s, 2H, NC$\underline{H}_2$), 7.20 (s, 1H, Ph), 7.75 (s, 2H, Ph) |
| **F23** | 1.23–1.30 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C$\underline{H}_3$)$_2$), 1.51 (s, 9H, C(C$\underline{H}_3$)$_3$), 2.87–3.09 (m, 1H, ArC$\underline{H}$), 3.83 (s, 2H, NC$\underline{H}_2$), 7.30–7.37 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.11–8.19 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F24** | 1.35 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.51 (s, 9H, C(C$\underline{H}_3$)$_3$), 3.83 (s, 2H, NC$\underline{H}_2$), 7.45–7.54 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.12–8.20 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F25** | 1.51 (s, 9H, C(C$\underline{H}_3$)$_3$), 3.84 (s, 2H, NC$\underline{H}_2$), 3.91–4.02 (d, 6H, Ar(OC$\underline{H}_3$)$_2$), 6.94–7.04 (d, 1H, $^3J_{HH}$ = 8 Hz, Ph), 8.05–8.20 (m, 2H, Ph) |
| **F26** | 0.78–0.97 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 1.42–1.51 (t, 3H, $^3J_{HH}$ = 7 Hz, CH$_2$C$\underline{H}_3$), 2.78–2.89 (m, 1H, NC$\underline{H}$), 3.72 (s, 2H, NC$\underline{H}_2$), 4.07–4.20 (qd, 2H, $^3J_{HH}$ = 7 Hz, OCH$_2$), 6.92–7.02 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.32–8.40 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F27** | 0.77–0.98 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.72–2.91 (m, 1H, NC$\underline{H}$), 3.73 (s, 2H, NC$\underline{H}_2$), 3.94–4.02 (d, 6H, Ar(OC$\underline{H}_3$)$_2$), 6.91–7.01 (d, 1H, $^3J_{HH}$ = 9 Hz, Ph), 8.08–8.21 (m, 2H, Ph) |
| **F28** | 0.73–1.02 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.38 (s, 6H, Ar(C$\underline{H}_3$)$_2$), 2.73–2.91 (m, 1H, NC$\underline{H}$), 3.72 (s, 2H, NC$\underline{H}_2$), 7.22 (s, 1H, Ph), 7.77 (s, 2H, Ph) |
| **F29** | 0.64–1.03 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.68–2.96 (m, 1H, NC$\underline{H}$), 3.74 (s, 2H, NC$\underline{H}_2$), 3.90 (s, 3H, OC$\underline{H}_3$), 6.97–7.00 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.18–8.56 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph) |
| **F30** | 0.78–1.00 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.73–2.94 (m, 1H, NC$\underline{H}$), 3.74 (s, 2H, NC$\underline{H}_2$), 3.94 (s, 9H, Ar(OC$\underline{H}_3$)$_3$), 7.86 (s, 2H, Ph) |
| **F31** | 0.70–1.02 (m, 7H, C$\underline{H}_2$C$\underline{H}_2$, CH$_2$C$\underline{H}_3$), 1.59–1.77 (m, 2H, $^3J_{HH}$ = 7 Hz, C$\underline{H}_3$C$\underline{H}_2$), 2.60–2.71 (t, 2H, $^3J_{HH}$ = 7 Hz, ArC$\underline{H}_2$), 2.80–2.90 (m, 1H, NCH), 3.72 (s, 2H, NC$\underline{H}_2$), 7.28–7.30 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph), 8.12–8.20 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph) |
| **F32** | 0.79–0.94 (m, 7H, CH$_2$C$\underline{H}_3$, C$\underline{H}_2$C$\underline{H}_2$), 1.26–1.40 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$CH$_3$), 1.57–1.70 (m, 2H, ArCH$_2$C$\underline{H}_2$), 2.63–2.71 (t, 2H, $^3J_{HH}$ = 7 Hz, ArC$\underline{H}_2$), 2.78–2.88 (m, 1H, NC$\underline{H}$), 3.72 (s, 2H, NC$\underline{H}_2$), 7.23–7.34 (d, 2H, $^3J_{HH}$ = 9 Hz, Ph), 8.13–8.18 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph) |
| **F33** | 0.83–0.91 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.74–2.90 (m, 1H, NC$\underline{H}$), 3.63 (s, 2H, NC$\underline{H}_2$), 3.81, 3.85 (s–s, 6H, Ar(OC$\underline{H}_3$)$_2$), 6.45–6.61 (m, 2H, Ph), 7.45 + 7.53 (m, 1H, Ph) |
| **F34** | 0.62–0.91 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.75–2.87 (m, 1H, NCH), 3.64 (s, 2H, NC$\underline{H}_2$), 6.94–7.93 (m, 9H, Ph) |
| **F35** | 0.68–0.96 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.74–2.90 (m, 1H, NC$\underline{H}$), 3.37 (s, 3H, OC$\underline{H}_3$), 3.53–3.59 (t, 2H, $^3J_{HH}$ = 4 Hz, CH$_3$OC$\underline{H}_2$), 3.72 (s, 2H, NC$\underline{H}_2$), 3.80–3.87 (t, 2H, $^3J_{HH}$ = 4 Hz, CH$_3$OCH$_2$C$\underline{H}_2$), 5.33 (s, 2H, ArOC$\underline{H}_2$), 7.24–7.91 (m, 4H, Ph) |
| **F36** | 0.69–0.96 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 2.74–2.88 (m, 1H, NC$\underline{H}$), 3.37 (s, 3H, OC$\underline{H}_3$), 3.52–3.59 (t, 2H, $^3J_{HH}$ = 4 Hz, CH$_3$OC$\underline{H}_2$), 3.70 (s, 2H, NCH$_2$), 3.79–3.86 (t, 2H, $^3J_{HH}$ = 5 Hz, CH$_3$OCH$_2$C$\underline{H}_2$), 5.35 (s, 2H, ArOC$\underline{H}_2$), 7.11, 7.13 (d, 2H, $^3J_{HH}$ = 8 Hz, Ph), 8.29, 8.32 (d, 2H, $J$ = 9 Hz, Ph) |

Hz, CH$_2$C$\underline{H}_3$), 2.0−2.16 (m, 2H, NHC$\underline{H}$), 3.31 (s, 2H, NC$\underline{H}_2$), 3.99−4.16 (qd, 2H, $^3J_{HH}$ = 7 Hz, OC$\underline{H}_2$).

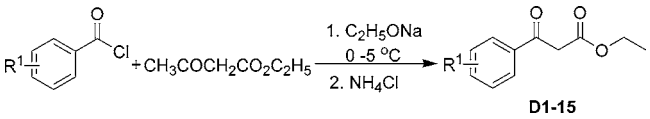
Compound **F** can be synthesized by acetylation of pyrrolidine-2,4-dione followed by the aroyl group's migration (*14*) or reaction of aroyl acetates with *N*-alkyl aminoacetates (*12*). We preferred the latter method to prepare the target products **B1** for its less toxic reagents and greater convenience. Intermediate **D** was reacted with **E** in refluxing absolute xylene to give the

**Table 4.** Herbicidal Activity of Compounds (Percent Inhibition)

| | *B. campestris* root test | | *E. crus-galli* cup test | |
|---|---|---|---|---|
| compd | 10 μg/mL | 100 μg/mL | 10 μg/mL | 100 μg/mL |
| **F1**[a] | 15 ± 1.1 | 62 ± 2.0 | 77 ± 0.3 | 77 ± 1.2 |
| **F2**[a] | 8 ± 0.6 | 86 ± 1.2 | 77 ± 0.2 | 78 ± 1.6 |
| **F3**[a] | 3 ± 1.0 | 59 ± 2.1 | 77 ± 0.7 | 78 ± 0.6 |
| **F4**[a] | 12 ± 0.0 | 71 ± 1.5 | 80 ± 0.4 | 80 ± 1.1 |
| **F5** | 8 ± 0.2 | 82 ± 2.7 | 79 ± 1.2 | 80 ± 0.4 |
| **F6** | 24 ± 2.1 | 34 ± 1.5 | 68 ± 2.1 | 76 ± 0.9 |
| **F7** | 3 ± 0.8 | 81 ± 0.8 | 22 ± 1.0 | 42 ± 0.8 |
| **F8** | 0 | 74 ± 0.6 | 0 | 39 ± 1.5 |
| **F9** | 0 | 85 ± 1.2 | 28 ± 1.1 | 44 ± 1.0 |
| **F10** | 10 ± 0.5 | 54 ± 1.2 | 74 ± 0.8 | 76 ± 1.4 |
| **F11** | 61 ± 2.3 | 69 ± 0.5 | 0 | 0 |
| **F12** | 60 ± 1.3 | 62 ± 0.8 | 0 | 64 ± 1.5 |
| **F13** | 60 ± 2.3 | 86 ± 0.6 | 27 ± 0.2 | 57 ± 1.0 |
| **F14** | 14 ± 3.0 | 29 ± 1.1 | 5.7 | 12 ± 2.1 |
| **F15** | 27 ± 2.8 | 69 ± 1.3 | 78 ± 0.4 | 80 ± 1.3 |
| **F16** | 0 | 81 ± 1.1 | 57 ± 0.7 | 67 ± 0.6 |
| **F17** | 7 ± 1.1 | 28 ±0.2 | 17 ± 1.5 | 52 ±1.7 |
| **F18** | 0 | 10 ± 0.5 | 8 ± 0.5 | 74 ± 1.6 |
| **F19** | 19 ± 2.0 | 51 ± 0.0 | 0 | 21 ± 1.3 |
| **F20** | 14 ± 2.8 | 88 ±1.2 | 36 ± 1.3 | 48 ± 1.1 |
| **F21**[a] | 5 ± 1.0 | 78 ± 1.3 | 79 ± 0.6 | 80 ± 1.5 |
| **F22**[a] | 41 ± 0.5 | 82 ± 1.0 | 1.0 ± 0.3 | 40 ± 2.8 |
| **F23** | 75 ± 1.5 | 83 ± 1.6 | 10 ± 0.5 | 18 ± 2.4 |
| **F24** | 64 ± 1.2 | 79 ± 1.3 | 4 ± 0.6 | 18 ± 1.6 |
| **F25** | 58 ± 2.3 | 70 ± 0.3 | 0 | 59 ± 2.5 |
| **F26** | 0 | 47 ± 0.5 | 78 ± 1.2 | 79 ± 1.4 |
| **F27** | 69 ± 1.3 | 72 ± 0.3 | 0 | 65 ± 1.7 |
| **F28** | 70 ± 1.9 | 86 ± 0.6 | 0 | 29 ± 2.6 |
| **F29** | 35 ± 1.5 | 70 ± 0.9 | 62 ± 0.6 | 66 ± 2.4 |
| **F30** | 45 ± 1.5 | 60 ± 0.3 | 4 ± 0.5 | 26 ± 0.6 |
| **F31** | 0 | 75 ± 0.5 | 8 ± 0.6 | 41 ± 0.7 |
| **F32** | 0 | 57 ± 0.6 | 5 ± 1.4 | 23 ± 1.0 |
| **F33** | 16 | 77 ± 0.2 | 78 ± 1.1 | 79 ± 0.6 |
| **F34** | 28 ± 1.1 | 80 ± 0.9 | 58 ± 2.4 | 66 ± 0.6 |
| **F35** | 0 | 35 ± 0.6 | 4 ± 1.2 | 33 ± 2.0 |
| **F36** | 19 ± 2.0 | 51 ± 1.1 | 0 | 12 ± 2.6 |

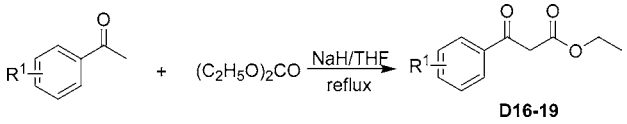
[a] These compounds and their herbicidal activities had been reported in ref *6*.

**Scheme 1**[a]



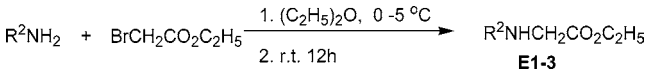

[a] Compounds **D1**–**15**: $R^1$ = 2-$CH_3$; 4-$CH_3$; 2-$CH_3O$; 4-$CH_3O$; 3,4-$(CH_3O)_2$; 3,5-$(CH_3)_2$; 4-$CH(CH_3)_2$; 2,4-$(CH_3)_2$; 3,4,5-$(CH_3O)_3$; 4-$C(CH_3)_3$; 2,4,5-$(CH_3O)_3$; 4-*n*-Pr; 4-$(CH_2)_4CH_3$; 4-$C_2H_5O$; 3-$C_6H_5O$.

**Scheme 2**[a]



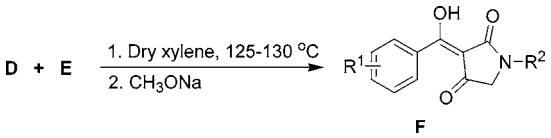

[a] Compounds **D16**–**19**: $R^1$ = 2-MEMO ($CH_3OCH_2CH_2OCH_2O$); 3-MEMO; 4-MEMO; 2, 4-$(CH_3O)_2$.

**Scheme 3**[a]




[a] Compounds E1–3: $R^2$ = *i*-Pr; *t*-Bu; cyclopropyl.

**Scheme 4**[a]




[a] Compounds **F1**–**19**: $R^1$ = 2-$CH_3$; 4-$CH_3$; 2-$CH_3O$; 4-$CH_3O$; 4-$C_2H_5O$; 3,4-$(CH_3O)_2$; 3,5-$(CH_3)_2$; 4-$CH(CH_3)_2$; 4-$C(CH_3)_3$; 2,4-$(CH_3)_2$; 3,4,5-$(CH_3O)_3$; 2,4,5-$(CH_3O)_3$; 4-*n*-Pr; 4-$(CH_2)_4CH_3$; 2,4-$(CH_3O)_2$; 3-$C_6H_5O$; 2-MEMO; 3-MEMO; 4-MEMO. $R^2$ = $CH(CH_3)_2$. Compounds **F20**–**25**: $R^1$ = 4-$CH_3$; 4-$CH_3O$; 3,5-$(CH_3)_2$; 4-$CH(CH_3)_2$; 4-$C(CH_3)_3$; 3,4-$(CH_3O)_2$. $R^2$ = $C(CH_3)_3$. Compounds **F26**–**36**: $R^1$ = 4-$C_2H_5O$; 3,4-$(CH_3O)_2$; 3,5-$(CH_3)_2$; 4-$CH_3O$; 3,4,5-$(CH_3O)_3$; 4-*n*-Pr; 4-$(CH_2)_4CH_3$; 2,4-$(CH_3O)_2$; 3-$C_6H_5O$; 3-MEMO; 4-MEMO. $R^2$ = cyclo-$C_3H_5$.

target compounds **F** (**Scheme 4**). This reaction was assumed to go through a nucleophilic addition/elimination reaction. During this process, an intermediate amide's formation and a cyclizative condensation were involved. According to this, when the $R^2$ substituent is bulky, the corresponding amide's yield would be lower ($R^2$ = *t*-Bu, **Table 2**), as a result of substituent steric hindrance.

**Structure−Activity Relationship.** The phenyl ring was substituted by different electron-donating groups $R^1$, and the related target products **F** were prepared. Their herbicidal activities were tested, and the results listed in **Table 4** show that when the substituents at the 2- and/or 4-position were smaller alkyl/alkoxy groups (such as methyl, methoxy, and ethoxy), the corresponding molecules always had a higher inhibition rate for *E. crus-galli* (compounds **F1**−**6**, **10**, **15**, **21**, **26**, and **33**) at 10 μg/mL. It was also found that when the 5-position hydrogen at the phenyl ring of **F15** was modified by a methoxy group, the target molecule **F12** had little inhibitory effect on *E. crus-galli*, indicating that a meta-position group (methyl or alkoxy) would not be essential for herbicidal activity. Thus, some compounds with higher inhibition rates for *E. crus-galli* were further bioassayed at a dosage of 1500 g/ha in the

**Table 5.** Herbicidal Activity of Compounds (Percent Inhibition) (Rate = 1500 g/ha)[a]

| | *B. campestris* | | *A. retroflexus* | | *E. crus-galli* | | *D. sanguinalis* | |
|---|---|---|---|---|---|---|---|---|
| compd | pre | post | pre | post | pre | post | pre | post |
| **F1** | 0 | 44 ± 1.5 | 50 ± 1.1 | 0 | 84 ± 0.3 | 76 ± 0.7 | – | – |
| **F2** | 24 ± 1.1 | 20 ± 0.4 | 11 ± 2.0 | 0 | 77 ± 0.6 | 67 ± 1.2 | – | – |
| **F3** | 0 | 21 ± 2.1 | 16 ± 1.0 | 0 | 93 ± 1.0 | 87 ± 0.5 | – | – |
| **F4** | 0 | 6 ± 1.0 | 11 ± 0.6 | 0 | 98 ± 0.3 | 75 ± 1.3 | – | – |
| **F5** | 0 | 0 | 0 | 0 | 100.0 ± 0.0 | 19 ± 2.0 | 98 ± 0.4 | 0 |
| **F10** | 20 ± 2.2 | 16 ± 2.3 | 13 ± 0.5 | 0 | 71 ± 1.2 | 66 ± 1.3 | – | – |
| **F16** | 0 | 0 | 0 | 9 ± 0.6 | 0 | 0 | 0 | 0 |
| **F21** | 21 ± 2.0 | 0 | 23 ± 0.8 | 0 | 93 ± 0.8 | 66 ± 1.2 | – | – |
| **F26** | 6 ± 1.7 | 0 | 0 | 13 ± 1.5 | 100 ± 0.0 | 0 | 42 ± 1.8 | 6 ± 1.5 |
| **F27** | 0 | 0 | 0 | 0 | 0 | 3 ± 1.0 | 11 ± 1.0 | 0 |
| **F29** | 0 | 0 | 0 | 0 | 81 ± 0.6 | 0 | 57 ± 2.8 | 0 |
| **F34** | 0 | 3 ± 1.0 | 0 | 9 ± 2.0 | 0 | 15 ± 1.6 | 0 | 10 ± 1.3 |

[a] Post, postemergence; pre, pre-emergence; –, not measured.

**Table 6.** Herbicidal Activity of Compounds (Percent Inhibition)

| compd | rate (g/ha) | pre-emergence treatment | |
|---|---|---|---|
| | | *E. crus-galli* | *D. sanguinalis* |
| **F1** | 750 | 68 ± 1.3 | 66 ± 1.2 |
| | 375 | 43 ± 1.1 | 30 ± 2.0 |
| **F2** | 750 | 22 ± 1.0 | 0 |
| **F4** | 750 | 92 ± 0.4 | 54 ± 1.6 |
| | 375 | 20 ± 1.8 | 38 ± 1.0 |
| **F5** | 750 | 98 ± 0.4 | 96 ± 0.4 |
| | 375 | 94 ± 0.6 | 94 ± 0.6 |
| | 187.5 | 52 ± 1.5 | 84 ± 0.7 |
| | 93.75 | 8 ± 2.0 | 22 ± 1.1 |
| **F15** | 750 | 100 ± 0.0 | 93 ± 0.1 |
| | 375 | 100 ± 0.0 | 77 ± 0.4 |
| | 187.5 | 93 ± 0.3 | 68 ± 1.7 |
| | 93.75 | 34 ± 1.8 | 0 |
| **F21** | 750 | 73 ± 1.1 | 58 ± 1.0 |
| | 375 | 0 | 8 ± 2.0 |
| **F26** | 750 | 99 ± 0.2 | 77 ± 0.3 |
| | 375 | 13 ± 2.0 | 33 ± 1.6 |
| | 187.5 | 0 | 18 ± 2.1 |
| **F29** | 750 | 69 ± 1.2 | 73 ± 1.0 |
| | 375 | 7 ± 1.6 | 69 ± 0.7 |
| sulcotrione | 750 | 100 ± 0.0 | 100 ± 0.0 |
| | 375 | 100 ± 0.0 | 100 ± 0.0 |
| | 187.5 | 93 ± 1.4 | 100 ± 0.0 |
| | 93.75 | 70 ± 2.0 | 100 ± 0.0 |

glasshouse on four herbs representative of monocotyledonous and dicotyledonous plants (**Table 5**).

From the biological assay results in **Table 5**, which summarize the herbicidal activity of the target compounds, some showed a much greater herbicidal activity in pre-emergence treatment than in postemergence treatment, especially for monocotyledonous plants *E. crus-galli* and *D. sanguinalis*. We analyzed the SAR according to the bioassay data in the pre-emergence treatment. When $R^2$ was not changed, the herbicidal activity rank for $R^1$ was 2-$CH_3$, 4-$CH_3$ < 4-$CH_3$, 4-$CH_3O$ < 4-$C_2H_5O$, 2,4-$(CH_3O)_2$; when $R^1$ was fixed, such as a 4-methoxy group, the herbicidal activity rank was cyclo-$C_3H_5$, *t*-Bu < *i*-$C_3H_7$ for *E. crus-galli*.

At the rate of 187.5 g/ha (**Table 6**), compounds **F5** and **F15** exhibited good herbicidal activities in comparison with sulcotrione and made the monocotyledonous plants *E. crus-galli* and *D. sanguinalis* bleached completely. Compared with the reported compounds of this kind (*15*), both of them showed excellent herbicidal activities. Compound **F4** exhibited excellent herbicidal activity at 1500 g/ha; however, its activity decreased remarkably when the dose was reduced to 375 g/ha.

In summary, we have demonstrated that when the substituents at the benzene ring of 3-[(α-hydroxy-substituted)benzylidene]-pyrrolidine-2,4-diones were electron-donating, especially at the 2- and/or 4-positions, these kinds of compounds presented excellent herbicidal activities. The results of the bioactivities of the new compounds against *E. crus-galli* and *D. sanguinalis* showed that some of the new compounds are effective herbicides compared to sulcotrione.

## LITERATURE CITED


(1) Wu, Y.-C.; Hu, F.-Z.; Yang, H.-Z. Research and development on the inhibitors of 4-hydroxyphenylpyruvate dioxygenase. *Nongyaoxue Xuebao* **2001**, *3*, 1−10 (in Chinese).

(2) Zhu, Y.-Q.; Hu, F.-Z.; Yang, H.-Z. Reviews on 4-hydroxyphenylpyruvate dioxygenase enzyme and the structure−activity relationships of its inhibitors. *Huaxue Tongbao* **2004**, *67*, w018/1−7 (in Chinese).

(3) Lee, D. L.; Prisbylla, M. P.; Cromartie, T. H.; Dagarin, D. P.; Howard, S. W.; Provan, W. M.; Ellis, M. K.; Fraser, T.; Mutter, L. C. The discovery and structural requirements of inhibitors of *p*-hydroxyphenylpyruvate dioxygenase. *Weed Sci.* **1997**, *45*, 601−609.

(4) Lee, D. L.; Knudsen, C. G.; Michaely, W. J.; Chin, H.-L.; Nguyen, N. H.; Carter, C. G.; Cromartie, T. H.; Lake, B. H.; Shribbs, J. M.; Fraser, T. The structure−activity relationships of the triketone class of *p*-hydroxyphenylpyruvate dioxygenase inhibiting herbicides. *Pestic. Sci.* **1998**, *54*, 377−384.

(5) Zhu, Y.-Q.; Hu, F.-Z.; Zou, X.-M.; Yao, C.-S.; Liu, B.; Li, Y.-H.; Yang, H.-Z. Synthesis of 1-benzyl-3-(α-hydroxy-(un)-substitutedbenzylidene)pyrrolidine-2,4-diones and biological activity. *Chin. J. Org. Chem.* **2005**, *25*, 419−423 (in Chinese).

(6) Zhu, Y.-Q.; Yao, C.-S.; Zou, X.-M.; Hu, F.-Z.; Liu, B.; Li, Y.-H.; Yang, H.-Z. The synthesis and herbicidal activity of 1-alkyl-3-(α-hydroxy-substituted benzylidene)pyrrolidine-2,4-diones. *Molecules* **2005**, *10*, 427−434.

(7) Meazza, G.; Scheffler, B. E.; Tellez, M. R.; Rimando, A. M.; Romagni, J. G.; Duke, S. O.; Nanayakkara, D.; Khan, I. A.; Abourashed, E. A.; Dayan, F. E. The inhibitory activity of natural products on plant *p*-hydroxyphenylpyruvate dioxygenase. *Phytochemistry* **2002**, *60*, 281−288.

(8) Zhu, Y.-Q.; Song, H.-B.; Li, J.-R.; Yao, C.-S.; Hu, F.-Z.; Zou, X.-M.; Yang, H.-Z. 1-Benzyl-3-(α-hydroxybenzylidene)pyrrolidine-2,4-dione. *Acta Crystallogr.* **2004**, *E60*, o196−o198.

(9) Zhu, Y.-Q.; Song, H.-B.; Yao, C.-S.; Gao, Y.; Hu, F.-Z.; Zou, X.-M.; Yang, H.-Z. 3-((α-hydroxy-2-methoxylbenzylidene)-1-isopropylpyrrolidine-2,4-dione. *Acta Crystallogr.* **2004**, *E60*, o599−o601.

(10) Speziale, A. J.; Jaworski, E. G. N-Substituted glycinate and alaninate eaters. *J. Org. Chem.* **1960**, *25*, 728−732.

(11) Morrison, G. C. Eur. Patent Appl. EP 0126651, 1984.

(12) Matsuo, K.; Kitaguchi, I.; Takata, Y.; Tanaka, K. Structure−activity relationships in tetramic acids and their copper(II) complexes. *Chem. Pharm. Bull.* **1980**, *28*, 2494−502.

(13) Wang, B.-L.; Duggleby, R. G.; Li, Z.-M.; Wang, J.-G.; Li, Y.-H.; Wang, S.-H.; Song, H.-B. Synthesis, crystal structure and herbicidal activity of mimics of intermediates of the KARI reaction. *Pest Manage. Sci.* **2005**, *61*, 407−412.

(14) Heather, J. B.; Milano, P. D. Acylated diketonic compounds. EP 0186117, 1986.

(15) Fischer, R.; Bretschneider, T.; Santel, H. J.; Luerssen, K.; Schmidt, R. R.; Erdelen, C. Preparation of 3-benzoylpyrrolidine-2,4-diones as insecticides and herbicides. (Bayer A.-G., Germany). DE 4223015, 1992.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