

The Synthesis and Herbicidal Activity of 1-Alkyl-3-(α -hydroxy-substituted benzylidene)pyrrolidine-2,4-diones

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Abstract: In the search for better herbicides a series of 1-alkyl-3-(α -hydroxy-(un)substituted benzylidene)pyrrolidine-2,4-diones were prepared and their structure-activity relationships studied. All their structures have been confirmed by $^1\text{H-NMR}$ and elemental analysis. The preliminary bioassay results indicated that some of them have high herbicidal activity against annual dicotyledonous and monocotyledonous plants.

Keywords: Pyrrolidine, herbicides, inhibition.

Introduction

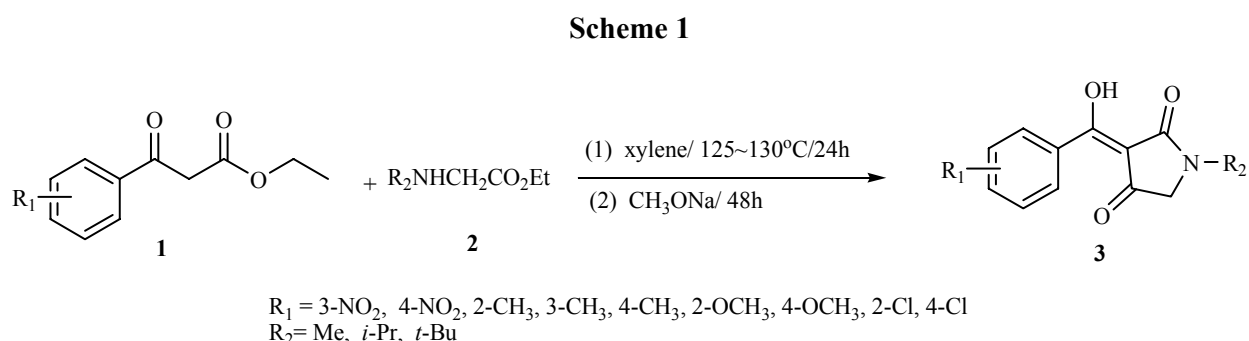
The inhibitors of 4-hydroxyphenylpyruvate dioxygenase (HPPD, EC 1.13.11.27) constitute a new kind of herbicides [1]. Generally, potent herbicides of this kind must possess the following structural features: 1) a tricarbonyl methane structure and one of the three carbonyl groups must be a substituted benzoyl group; 2) the compound must be able to enolise so that the enolate is capable of inhibiting HPPD enzyme by competitive combination with Fe^{2+} —the reaction center of HPPD enzyme [2]. Recently, we observed that the 3-acyltetramic acids form an expanding group of antibiotics and pigments derived from microorganisms [3]. They display a range of biological activities [4] and all compounds of this kind possess a tricarbonyl methane structure and can essentially enolise completely (the chemical shifts of their enolic hydroxyls were larger than 10). Tests of their antimicrobial activities indicated that the structure of the acyl substituent at the 3-position and possession of a 3-

acyltetramic acid moiety as the tricarbonylmethane structure is important for many typical antibiotics [4-5]. These characteristics stimulated us to study this kind of compounds in the search for new herbicides. In our previous study [6], we synthesized a series of 1-benzyl-3-(α -hydroxy-(un)substituted benzylidene)-pyrrolidine-2,4-diones and found there existed to some extent structure-activity relationships between them. Furthermore and importantly, these compounds possessed both growth inhibiting and bleaching properties. The combination of both features could lead to the discovery of new potential herbicides. In this paper, we report the design and synthesis of the title compounds **3**, based on the HPPD structure and its reactivity with chemical compounds [7-9], which were found to have herbicidal activities about 100 times those of the compounds reported before [6]. Their structure-activity relationships are discussed.

Results and Discussion

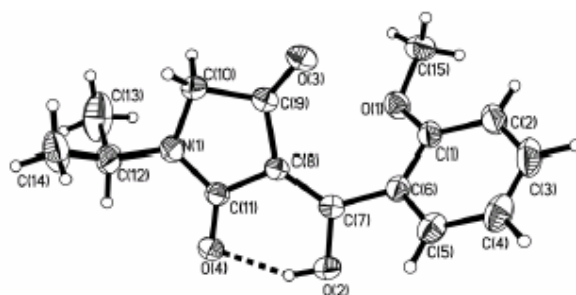
Synthesis and characterization of target compounds

The synthesis route is shown in Scheme 1.



Compounds **3a**~**3w** were identified by IR and $^1\text{H-NMR}$. The measured elemental analyses are also consistent with the corresponding calculated ones. In the IR spectra there are medium or weak absorption bands for the enol group ($\nu_{\text{O-H}}$) at around 3400cm^{-1} and the three carbonyl groups show relatively strong absorption bands at around 1700cm^{-1} , 1680 and 1580cm^{-1} . In the $^1\text{H-NMR}$ spectra of these compounds, no signals are found for the proton of CH group connecting the three carbonyl groups; this is evidence that an enol isomer was formed and as a result of proton exchange, the enol proton peak was not observed. The enol form was also confirmed through the single crystal X-ray diffraction of compound **3k** (whose molecular structure is shown in Figure 1)[10].

Figure 1 Molecular structure for the compound (**3k**) with the atomic numbering scheme.



Biological evaluation

The herbicidal activities of the target compounds were determined with *Brassica napus* and *Echinochloa crusgalli* (L.) Beauv as samples of annual dicotyledonous and monocotyledonous plants, respectively, by the method reported by Yang *et al.* [11]. The results are summarized in Table 1 and they show that in these preliminary tests, most of the target compounds (such as **3l**, **3m**, **3n**, **3o**, **3s**, **3t** and **3u**) have inhibiting, and to some extent, bleaching activity and exhibit better efficacy against *Brassica napus* and *Echinochloa crusgalli*(L.) Beauv on the whole, with inhibition rates against these species ranging between 74% to 83% at 100 ug/L.

Table 1 The biological activity(%) of compounds **3a** ~ **3w** against *Brassica napus* and *Echinochloa crusgalli* (L.) Beauv

Cpd No	R1 ; R2	Brassica napus(ug/mL, inhibition %)		Echinochloa crusgalli (L.) Beauv(ug/mL, inhibition %)		
		10	100	10	100	Bleaching result at 100 ug/mL *
3a	3-NO ₂ ; Me	0	22.4	5.2	42.8	+
3b	4-NO ₂ ; Me	5.1	40.9	9.0	51.9	+
3c	4-Cl ; Me	15.8	90.5	9.4	50.1	+
3d	2-CH ₃ ; Me	0	44.4	31.2	78.3	++
3e	3-CH ₃ ; Me	14.0	64.0	25.3	68.3	++
3f	4-OCH ₃ ; Me	7.9	50.7	16.2	78.8	++
3g	3-NO ₂ ; i-Pr	10.2	70.3	0	42	+
3h	4-NO ₂ ; i-Pr	4.5	34.2	0	1.6	-
3i	2-Cl ; i-Pr	38.9	66.8	51	77.9	++
3j	4-Cl ; i-Pr	16	77.2	25.1	68	++
3k	2-OCH ₃ ; i-Pr	3.0	58.7	77.3	78.1	+++
3l	4-OCH ₃ ; i-Pr	11.9	71	79.6	80	+++
3m	2-CH ₃ ; i-Pr	15.2	62.4	76.9	77.3	+++
3n	3-CH ₃ ; i-Pr	3.3	82.1	49.2	75.5	+++
3o	4-CH ₃ ; i-Pr	8.1	86.4	76.8	78.4	+++
3p	3-NO ₂ ; t-Bu	22.1	80.1	0	0.5	-
3q	4-NO ₂ ; t-Bu	1.8	48.1	0	9.8	-
3r	4-Cl; t-Bu	13.8	98	0.4	20.8	-
3s	2-OCH ₃ ; t-Bu	41.2	69.5	74.9	82.9	++
3t	4-OCH ₃ ; t-Bu	5.4	77.7	78.7	80.3	++
3u	2-CH ₃ ; t-Bu	21.1	74.9	63.6	74.4	++
3v	3-CH ₃ ; t-Bu	24.9	85.0	4.9	48.5	+
3w	4-CH ₃ ; t-Bu	13.5	88.1	36.3	48	+
Sulcotrione**		3.5	38.1	29.4	45.1	+++

* - no change ; + weak ; ++ moderate ; +++ high; ** 2-(2-chloro-4-mesylbenzoyl)cyclohexane-1,3-dione

At the lower test concentration (10 ug/L), the compounds mentioned above showed higher biological activity against *Echinochloa crusgalli* (L.) Beauv and lower biological activity against *Brassica napus*. The highest inhibition rate against *Echinochloa crusgalli* (L.) Beauv is 79.6% at 10 ug/L (the rates are 100 times of that of these compounds previous reported [6]). This indicated that these compounds had better selectivity. The data in Table 1 also show that most of the target compounds have much higher inhibiting activity and slightly weaker bleaching activity than the standard sulcotrione under the test conditions.

In Table 1, as far as the relationships between the structure and the activity is concerned, it also shows that when R_1 is the same and R_2 is changed, the inhibition ranking is $Me < t-Bu \leq i-Pr$, indicating that alkyl groups both larger and smaller in size than an iso-propyl group do not favor the target compounds' combination with Fe^{2+} —the reaction center of HPPD; when R_2 is same, and R_1 is changed, the result that the inhibition ranking is electron-withdrawing group < electron-donating group shows that electron-donating groups are propitious to the enol-isomer form, and furthermore enhance the target compounds' chance of combining with the center of HPPD. The above phenomena are more obvious and shows that these target compounds not only have bleaching activity, but they also have inhibiting activity.

Conclusions

Twenty-three novel title compounds containing a tricarbonylmethane unit have been synthesized. Their structures have been verified by 1H -NMR and IR spectral data, crystal x-ray diffraction and elemental analysis. Under the test conditions most of them show better inhibition activity and some of them show a similar degree of bleaching activity as a sulcotrione standard, and compared to the commercial agent the herbicidal activities of this type of compounds are encouraging. It is possible that the combination of the two action modes lead to their better herbicidal activity. Further work is in progress.

Acknowledgements

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Experimental

Materials and instruments

Melting points were determined using a Yanaco MP-241 apparatus and are uncorrected. Infrared spectra were recorded on a Shimadzu IR-435 spectrophotometer as thin films or potassium bromide tablets. 1H -NMR spectra were measured on a Bruker AC-P500 instrument (300MHz) using tetramethylsilane as an internal standard and deuteriochloroform as solvent. Elemental analyses were performed on a Yanaco MT-3CHN elemental analyzer. All agents were on analytical grade and were used without further purification. The crystal structure determination of compound **3k** and its crystal structure were described in reference [10]. The intermediates **1** were prepared according to the

literature method [6]. All of the related data were listed in that reference. The intermediates **2** were prepared according to the literature [12] ($R_2 = i\text{-Pr}$, 40%, 51~53°C/4.5mmHg, $n_d^{25} = 1.4170$; $R_2 = t\text{-Bu}$, 65.4%, 59~61°C/2 mmHg, $n_d^{25} = 1.4225$).

General procedure for the synthesis of compounds 3a~3w: Preparation of 1-methyl-3-(α -hydroxy-3'-nitrobenzylidene)pyrrolidine-2,4-dione (3a)

A mixture of **1** ($R_1 = 3\text{-NO}_2$, 4.11 mmol) and ethyl benzylamino acetate (**2**, $R_2 = \text{Me}$) (4.30 mmol) in dry xylene (15 mL) was heated at 125–130 °C with stirring for 20 hours. 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 hours, 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 2N 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 **3a**, which was purified by flash column chromatography on silica gel, using 1:1 (v:v) ethyl acetate-petroleum ether as the eluent to afford the target product as white crystals (1.0g, 92.8%) with m.p. 145~146 °C; IR (KBr) cm^{-1} 3443(O-H), 1678, 1575, 1520(C=O); $^1\text{H-NMR}$ δ : 3.06 (s, 3H, N-CH₃), 3.78 (s, 2H, C-CH₂-N), 8.22–8.33 (m, 4H, C₆H₄); Anal. Calc. for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_5$ (262.21) C 54.96, H 3.84, N 10.68; Found: C 55.01, H 3.89, N 10.51. The twenty two other title compounds **3b~3x** were synthesized in the same manner.

1-methyl-3-(α -hydroxy-4'-nitrobenzylidene)pyrrolidine-2,4-dione (3b): Yield 67.0%; m.p. 167~169°C; IR (KBr) cm^{-1} 3450(O-H), 1690, 1585, 1520 (C=O); $^1\text{H-NMR}$ δ : 3.06 (s, 3H, N-CH₃), 3.78 (s, 2H, C-CH₂-N), 8.22–8.33(m, 4H, C₆H₄); Anal. Calc. for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_5$ (262.21) C 54.96, H 3.84, N 10.68; Found: C 54.83, H 3.99, N 10.72.

1-methyl-3-(α -hydroxy-4'-chlorobenzylidene)pyrrolidine-2,4-dione (3c). Yield 57.3%; m.p. 104~105 °C; IR (KBr) cm^{-1} 3463(O-H), 1712, 1670, 1598(C=O); $^1\text{H-NMR}$ δ : 3.10 (s, 3H, NCH₃), 3.81 (s, 2H, CCH₂N), 7.46, 7.49, 8.21, 8.24 (d-d, 4H, J=9.04 Hz, C₆H₄); Anal. Calc. for $\text{C}_{12}\text{H}_9\text{ClNO}_3$ (251.66) C 57.27, H 4.00, N 5.57; Found C 57.21, H 4.07, N 5.57.

1-methyl-3-(α -hydroxy-2'-methylbenzylidene)pyrrolidine-2,4-dione (3d). Yield 52.2%; yellow liquid; IR (KBr) cm^{-1} 3422 (O-H), 1719, 1657, 1620 (C=O); $^1\text{H-NMR}$ δ : 2.32 (s, 3H, ArCH₃), 3.02 (s, 3H, N-CH₃), 3.67 (s, 2H, CCH₂N), 7.13–7.42 (m, 4H, C₆H₄); Anal. Calc. for $\text{C}_{13}\text{H}_{13}\text{NO}_3$ (231.24) C 67.52, H 5.67, N 6.06; Found C 67.42, H 5.51, N 6.01.

1-methyl-3-(α -hydroxy-3'-methylbenzylidene)pyrrolidine-2,4-dione (3e). Yield 86.5%; red liquid; IR (KBr) cm^{-1} 3435 (O-H), 1720, 1654, 1621 (C=O); $^1\text{H-NMR}$ δ : 2.36 (s, 3H, ArCH₃), 3.02 (s, 3H, N-CH₃), 3.72 (s, 2H, CCH₂N), 7.23–7.39, 7.83–8.03 (m, 4H, C₆H₄); Anal. Calc. for $\text{C}_{13}\text{H}_{13}\text{NO}_3$ (231.24) C 67.52, H 5.67, N 6.06; Found C 67.60, H 5.59, N 6.05.

1-methyl-3-(α -hydroxy-4'-methoxybenzylidene)pyrrolidine-2,4-dione (3f). Yield 62.9%; m.p. 96~97 °C; IR (KBr) cm^{-1} 3419 (O-H), 1717, 1652, 1616 (C=O); $^1\text{H-NMR}$ δ : 3.00 (s, 3H, NCH_3), 3.71 (s, 2H, CCH_2N), 3.81 (s, 3H, OCH_3), 6.88, 6.99, 8.28, 8.31 (d-d, 4H, $J=9.04$ Hz, C_6H_4); Anal. Calc. for $\text{C}_{13}\text{H}_{13}\text{NO}_4$ (247.24) C 63.15, H 5.30, N 5.67; Found C 63.14, H 5.43, N 5.78.

1-i-propyl-3-(α -hydroxy-3'-nitrobenzylidene)pyrrolidine-2,4-dione (3g). Yield 74.8%; m.p. 136~137 °C; IR(KBr) cm^{-1} 3453 (O-H), 1688, 1595, 1532 (C=O); $^1\text{H-NMR}$ δ : 1.21(d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 3.72 (s, 2H, $\text{C-CH}_2\text{-N}$), 4.38-4.68 (m, 1H, $J=6.78\text{Hz}$, CH), 7.51-7.70, 8.28-8.60, 9.02-9.13 (m, 4H, $J=8.29$ Hz, C_6H_4); Anal. Calc. for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_5$ (290.26) C 57.93, H 4.86, N 9.65; Found: C 57.96, H 5.08, N 9.75.

1-i-propyl-3-(α -hydroxy-4'-nitrobenzylidene)pyrrolidine-2,4-dione (3h). Yield 69.2%; m.p. 146~147 °C; IR (KBr) cm^{-1} 3463 (O-H), 1693, 1610, 1553 (C=O); $^1\text{H-NMR}$ δ : 1.22 (d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 3.71 (s, 2H, $\text{C-CH}_2\text{-N}$), 4.47-4.57 (m, 1H, $J=6.78\text{Hz}$, CH), 7.91-7.94, 8.23-8.31 (m, 4H, $J=9.04$ Hz, C_6H_4); Anal. Calc. for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_5$ (290.26) C 57.93, H 4.86, N 9.65; Found C 57.94, H 4.73, N 9.65.

1-i-propyl-3-(α -hydroxy-2-chlorobenzylidene)pyrrolidine-2,4-dione (3i). Yield 37.2%; m.p. 103~104 °C. IR (KBr) cm^{-1} 3418(O-H), 1726, 1656, 1561(C=O). $^1\text{H-NMR}$ δ : 1.27-1.29 (d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 3.71 (s, 2H, CCH_2N), 4.50-4.74 (m, 1H, $J=6.78\text{Hz}$, CH), 7.31-7.62 (m, 4H, $J=9.04$ Hz, C_6H_4). Anal. Calc. for $\text{C}_{14}\text{H}_{14}\text{ClNO}_3$ (279.71) C 60.11, H 5.04, N 5.01; Found C 60.22, H 5.09, N 5.11.

1-i-propyl-3-(α -hydroxy-4'-chlorobenzylidene)pyrrolidine-2,4-dione (3j). Yield 73.1%; m.p. 134~135 °C; IR (KBr) cm^{-1} 3405 (O-H), 1694, 1587, 1544 (C=O); $^1\text{H-NMR}$ δ : 1.27 (d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 3.76 (s, 2H, CCH_2N), 4.54-4.66 (m, 1H, $J=6.78\text{Hz}$, CH), 7.46-7.48, 8.21-8.28 (m, 4H, C_6H_4); Anal. Calc. for $\text{C}_{14}\text{H}_{14}\text{ClNO}_3$ (279.71) C 60.11, H 5.04, N 5.01; Found C 60.22, H 5.09, N 5.11.

1-i-propyl-3-(α -hydroxy-2'-methoxybenzylidene)pyrrolidine-2,4-dione (3k). Yield 79.9%; m.p. 99~100 °C; IR (KBr) cm^{-1} 3441 (O-H), 1741, 1600, 1559 (C=O); $^1\text{H-NMR}$ δ : 1.25 (d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 3.66 (s, 2H, CCH_2N), 3.86 (s, 3H, Ar-OCH_3), 4.57-4.62 (m, 1H, $J=6.78\text{Hz}$, CH), 7.00-7.06, 7.45-7.53 (m, 4H, C_6H_4); Anal. Calc. for $\text{C}_{15}\text{H}_{17}\text{NO}_4$ (275.29) C 65.44, H 6.22, N 5.09; Found C 65.45, H 6.27, N 4.98.

1-i-propyl-3-(α -hydroxy-4'-methoxybenzylidene)pyrrolidine-2,4-dione (3l). Yield 85.4%; m.p. 145~146 °C; IR (KBr) cm^{-1} 3463 (O-H), 1695, 1590, 1546 (C=O); $^1\text{H-NMR}$ δ : 1.17 (d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 3.65 (s, 2H, $\text{C-CH}_2\text{-N}$), 3.82 (s, 3H, Ar-OCH_3), 4.45-4.55 (m, 1H, $J=6.78\text{Hz}$, CH), 6.89, 6.92, 8.27, 8.30 (d-d, 4H, $J=9.04\text{Hz}$, C_6H_4); Anal. Calc. for $\text{C}_{15}\text{H}_{17}\text{NO}_4$ (275.29) C 65.44, H 6.22, N 5.09; Found C 65.39, H 6.25, N 5.07.

1-i-propyl-3-(α -hydroxy-2'-methylbenzylidene)pyrrolidine-2,4-dione (3m). Yield 90.8%; m.p. 79~80 °C; IR (KBr) cm^{-1} 3427 (O-H), 1719, 1646, 1601 (C=O); $^1\text{H-NMR}$ δ : 1.37 (d, 6H, $J=6.78\text{Hz}$, $\text{C}(\text{CH}_3)_2$), 2.42 (s, 3H, Ar-CH_3), 3.70 (s, 2H, CCH_2N), 4.56-4.66 (m, 1H, $J=6.78\text{Hz}$, CH), 7.28-7.49 (m,

4H, C₆H₄); Anal. Calc. for C₁₅H₁₇NO₃ (259.29) C 69.48, H 6.61, N 5.40; Found C 69.56, H 6.58, N 5.35.

1-i-propyl-3-(α-hydroxy-3'-methylbenzylidene)pyrrolidine-2,4-dione (3n). Yield 75.7%; m.p. 64~65 °C; IR (KBr) cm⁻¹ 3477 (O-H), 1745, 1685, 1591 (C=O); ¹H-NMR δ: 1.18 (d, 6H, J=6.78Hz, C(CH₃)₂), 2.24 (s, 3H, Ar-CH₃), 3.68 (s, 2H, CCH₂N), 4.48-4.55 (m, 1H, J=6.78Hz, CH), 7.19-7.95 (m, 4H, C₆H₄); Anal. Calc. for C₁₅H₁₇NO₃ (259.29) C 69.48, H 6.61, N 5.40; Found C 69.35, H 6.45, N 5.48.

1-i-propyl-3-(α-hydroxy-4'-methylbenzylidene)pyrrolidine-2,4-dione (3o). Yield 85.3%; m.p. 101~102 °C; IR (KBr) cm⁻¹ 3378 (O-H), 1692, 1652, 1590 (C=O); ¹H-NMR δ: 1.37 (d, 6H, J=6.78Hz, C(CH₃)₂), 2.45 (s, 3H, Ar-CH₃), 3.74 (s, 2H, CCH₂N), 4.57-4.62 (m, 1H, J=6.78Hz, CH), 7.28-7.49 (m, 4H, C₆H₄); Anal. Calc. for C₁₅H₁₇NO₃ (259.29) C 69.48, H 6.61, N 5.40; Found C 69.69, H 6.65, N 5.56.

1-t-butyl-3-(α-hydroxy-3'-nitrobenzylidene)pyrrolidine-2,4-dione (3p). Yield 35.1%; m.p. 168~169 °C. IR (KBr) cm⁻¹ 3463(O-H), 1698, 1651,1557(C=O). ¹H-NMR δ: 1.55 (s, 9H, C(CH₃)₃), 3.91 (s, 2H, C-CH₂-N), 7.61-7.85, 8.35-8.67, 9.07-9.20 (m, 4H, J=8.29 Hz, C₆H₄); Anal. Calc. for C₁₅H₁₆N₂O₅ (304.29) C 59.20, H 5.30, N 9.31; Found C 59.31, H 5.28, N 9.20.

1-t-butyl-3-(α-hydroxy-4'-nitrobenzylidene)pyrrolidine-2,4-dione (3q). Yield 39.6%; m.p. 142~144 °C; IR (KBr) cm⁻¹ 3463 (O-H), 1698, 1651, 1557 (C=O); ¹H-NMR δ: 1.46 (s, 9H, C(CH₃)₃), 3.81 (s, 2H, C-CH₂-N), 8.15-8.38 (m, 4H, C₆H₄); Anal. Calc. for C₁₅H₁₆N₂O₅ (304.29) C 59.20, H 5.30, N 9.31; Found C 61.50, H 4.85, N 11.28.

1-t-butyl-3-(α-hydroxy-4'-chlorobenzylidene)pyrrolidine-2,4-dione (3r). Yield 73.1%; m.p. 134~135 °C; IR (KBr) cm⁻¹ 3405(O-H), 1694 1587,1544(C=O). ¹H-NMR δ : 1.27 (d, 6H, J=6.78Hz, C(CH₃)₂), 3.76 (s, 2H, CCH₂N), 4.54-4.66 (m, 1H, J=6.78Hz, CH), 7.46-7.48, 8.21-8.28 (m, 4H, C₆H₄); Anal. Calc. for C₁₄H₁₄ClNO₃ (279.71) C 60.11, H 5.04, N 5.01; Found C 60.22, H 5.09, N 5.11.

1-t-butyl-3-(α-hydroxy-2'-methoxybenzylidene)pyrrolidine-2,4-dione (3s). Yield 30%; m.p. 66~67 °C; IR (KBr) cm⁻¹ 3381 (O-H), 1748, 1711, 1624 (C=O); ¹H-NMR δ: 1.52 (s, 9H, C(CH₃)₃), 3.88 (s, 3H, Ar-OCH₃), 3.78 (s, 2H, C-CH₂-N), 6.99-7.06, 7.44-7.48 (m, 4H, J=9.04Hz, C₆H₄); Anal. Calc. for C₁₆H₁₉NO₄ (289.32) C 66.42, H 6.62, N 4.84; Found C 66.35, H 6.57, N 5.01.

1-t-butyl-3-(α-hydroxy-4'-methoxybenzylidene)pyrrolidine-2,4-dione (3t). Yield 40.7%; m.p. 117~118 °C; IR (KBr) cm⁻¹ 3431 (O-H), 1743, 1683, 1594 (C=O); ¹H-NMR δ: 1.43 (s, 9H, C(CH₃)₃), 3.80 (s, 3H, Ar-OCH₃), 3.75 (s, 2H, C-CH₂-N), 6.88, 6.91, 8.25, 8.28 (d-d, 4H, J=9.04Hz, C₆H₄); Anal. Calc. for C₁₆H₁₉NO₄ (289.32) C 66.42, H 6.62, N 4.84; Found C 66.32, H 6.67, N 5.04.

1-t-butyl-3-(α-hydroxy-2'-methylbenzylidene)pyrrolidine-2,4-dione (3u). Yield 60.4%; m.p. 69~70 °C; IR (KBr) cm⁻¹ 3430 (O-H), 1718, 1651, 1611 (C=O); ¹H-NMR δ: 1.45 (s, 3H, NCH₃), 2.33 (s, 2H, CCH₂N), 3.72 (s, 3H, OCH₃), 7.16-7.38 (m, 4H, J=6.028 Hz, C₆H₄); Anal. Calc. for C₁₆H₁₉NO₃ (273.32) C 70.31, H 7.01, N 5.12; Found C 70.16, H 6.98, N 5.08.

1-t-butyl-3-(α -hydroxy-3'-methyl benzylidene)pyrrolidine-2,4-dione (3v). Yield 53.8%; m.p. 137~138 °C; IR (KBr) cm^{-1} 3412 (O-H), 1708, 1648, 1564 (C=O); $^1\text{H-NMR}$ δ : 1.53 (s, 3H, NCH_3), 2.44 (s, 2H, CCH_2N), 3.84 (s, 3H, OCH_3), 7.32-8.04 (m, 4H, C_6H_4); Anal. Calc. for $\text{C}_{16}\text{H}_{19}\text{NO}_3$ (273.32) C 70.31, H 7.01, N 5.12; Found C 70.32, H 7.08, N 5.15.

1-t-butyl-3-(α -hydroxy-4'-methylbenzylidene)pyrrolidine-2,4-dione (3w). Yield 32.4%; m.p. 124~125 °C; IR (KBr) cm^{-1} 3378 (O-H), 1709, 1665, 1588 (C=O); $^1\text{H-NMR}$ δ : 1.53 (s, 3H, NCH_3), 2.44 (s, 2H, CCH_2N), 3.84 (s, 3H, OCH_3), 7.26-8.14 (m, 4H, C_6H_4); Anal. Calc. for $\text{C}_{16}\text{H}_{19}\text{NO}_3$ (273.32) C 70.31, H 7.01, N 5.12; Found C 70.30, H 6.99, N 5.15.

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