Synthesis of 2-Dihydrooxadiazolinyl Chromones

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Reactions of the substituted 2-formyl chromones with aroylhydrazines gave corresponding 2-(aroylhydrazonomethylidyne) chromones. Then 2-(3′-acetyl-5′-aryl-2′,3′-dihydro-1′,3′,4′-oxadiazol-2′-yl) chromones were prepared by these 2-(aroylhydrazonomethylidyne) chromones under refluxing with Ac_2O. All target compounds were characterized through elemental analysis and IR, ^{1}H NMR, MS.

Keywords: Oxadiazoline; Chromone; Synthesis.

INTRODUCTION

There are a lot of compounds which include a chromone nucleus in nature. They have been interesting because of their special framework and wide biomedical activities, e.g., antimicrobial, antiallergic, anti-inflammatory, antitumor, anti-spastic, reducing bloodsugar and fats in blood,[1-7] and so on. Heterocyclic compounds, such as 1,3,4-oxadiazole, also have versatile and significant biological activities as fungicides, antimicrobes, insecticides, as well as anticonvulsives.[8,9] The derivatives of 1,3,4-oxadiazole which are linked with quinoline[10] and theophylline[11] have been reported. Acylhydrazines prove to be suitable trapping agents for the isolation of oxo compounds, and acylhydrazones due to their biological activities can be regarded as potential pharmacons.[12] A series of investigations on combining these components often exhibited some novel biological activities in addition to the above mentioned compounds. In view of this, the synthesis of 2-heterocyclic linked chromones attracted our interest.

In this paper we describe the synthesis and physical characterization of new 2-heterocyclic linked chromones **22**~**41**. And all the new compounds were characterized by elemental analysis and IR, ^{1}H NMR, MS spectral data. Biological activities are being tested.

The 2-formyl chromones were prepared from 2-acetyl phenol. 2-acetyl phenol could condense with ethyl acetate under sodium catalyzation, so 2-acetylacetyl phenol could be prepared though their sodium salt. Then substituted 2-methyl chromones were formed by 2-acetylacetyl phenol under catalytic amounts of concentrated hydrochloric acid and HOAc.[6] The substituted 2-methyl chromones reacted with *p*-nitrosodimethylaniline, which gave corresponding nitrones. Nitrones were treated with dilute sulphuric acid, then the corresponding 2-formyl chromones were formed.[11] Reactions of the substituted 2-formyl chromones with aroylhydrazines gave corresponding 2-(aroylhydrazonomethylidyne) chromones (**2**~**21**). Then 2-(3′-acetyl-5′-aryl-2′,3′-dihydro-1′,3′,4′-oxadiazol-2′-yl) chromones were (**22**~**41**) prepared by these 2-(aroylhydrazonomethylidyne) chromones refluxing under Ac_2O. We synthesized the title compounds according to the following route (Scheme I, Table 1).

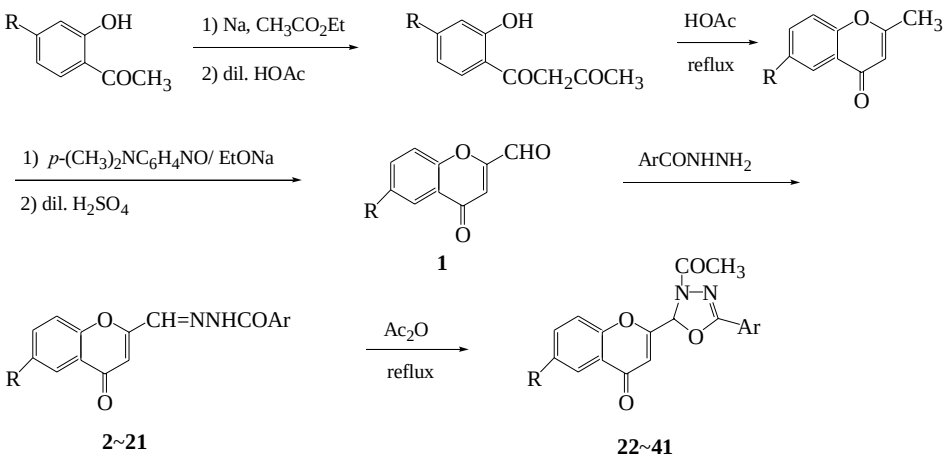
RESULTS AND DISCUSSION

2-Formyl chromones were prepared from 2-methyl

Table 1. The Target Compounds

Compd.	R	Ar
2, 22	H	C_6H_5
3, 23	H	*p*-Cl-C_6H_4
4, 24	H	*o*-Cl-C_6H_4
5, 25	H	*p*-CH_3O-C_6H_4
6, 26	H	*p*-NO_2-C_6H_4
7, 27	CH_3	C_6H_5
8, 28	CH_3	*p*-Cl-C_6H_4
9, 29	CH_3	*o*-Cl-C_6H_4
10, 30	CH_3	*p*-CH_3O-C_6H_4
11, 31	CH_3	*p*-NO_2-C_6H_4
12, 32	Cl	C_6H_5
13, 33	Cl	*p*-Cl-C_6H_4
14, 34	Cl	*o*-Cl-C_6H_4
15, 35	Cl	*p*-CH_3O-C_6H_4
16, 36	Cl	*p*-NO_2-C_6H_4
17, 37	Br	C_6H_5
18, 38	Br	*p*-Cl-C_6H_4
19, 39	Br	*o*-Cl-C_6H_4
20, 40	Br	*p*-CH_3O-C_6H_4
21, 41	Br	*p*-NO_2-C_6H_4

Scheme I



chromones. In other articles the preparation of 2-formyl chromones had two methods. One method was using selenium dioxide, 2-methyl at chromone nucleus to carbonyl could be oxidized selectively.[12] The other was an indirect conversion with two steps reaction. The first step involved conversion of 2-methyl chromones into corresponding nitrones, which on treatment with dilute sulphuric acid, in the second step gave 2-formyl chromones. Because with the first method there must be separation by chromatography and with a lot of by-products, this was inconvenient. We selected the second method, but it wasn't reported in detail. We made certain of the minimal quantity of solvent and the reaction time, and improved the yield.

2-Formyl chromones could react with aroylhydrazine easily, then give corresponding aroylhydrazonomethylidyne chromones. However, 4-carbonyl at a chromone nucleus reacted with aroylhydrazine, too, under certain conditions. But 2-formyl at a chromone nucleus is more active than 4-carbonyl at a chromone. So we controlled the condition of the reaction so that aroylhydrazine reacted with 2-formyl at the chromone only and didn't react with 4-carbonyl at the chromone. We adopted the room temperature and equimolecular quantities material ratio. Under glacial acetic acid catalyzation, our expected results could separate out rapidly as precipitation. And we found that the yield was higher when aroylhydrazine linked electron-attracting radicals. This could be the character of radical effect on the nucleophilic character of reactant and the electron density of the product.

When the ring closure of 2-(aroylhydrazonomethylidyne) chromones was taken through the reacting with acetic anhydride, the dosage of acetic anhydride was more than others. Because the solubility of this kind of 2-(aroylhydrazomethylidyne) chromones was low.

The IR spectra of compounds **22~41** clearly differ from the spectra of corresponding 2-(aroylhydrazomethylidyne) chromones **2~21**. The compounds **2~21** exhibited a wide peak at 3280-3090 cm^{-1} (NH). But for the compounds **22~41**, the peaks in these bands were devoid. At the same time, the IR spectra of compounds **22~41** shows strong absorption at 1640-1635 cm^{-1} (pyrone C=O) and 1685-1680 cm^{-1} ($COCH_3$), and exhibited strong absorption at 1600-1598 cm^{-1} (C=N).

The ^{1}H NMR spectra of compounds **22~41** are in perfect agreement with the suggested structures of target compounds. The ^{1}H NMR spectra of **22~41**, as a representative, exhibited signals at δ 2.3 ($COCH_3$, s), δ 6.8 (CH), δ 7.3 (H-3, s). Then chromone proton H-5 displayed as a double peak at δ 8.1 (coupling with H-7, $^4J \sim 2.4$ Hz), and H-7 showed d × d peaks because this proton coupled with H-5 and H-8, respectively ($^4J \sim 2.4$ Hz, $^3J \sim 8$ Hz).

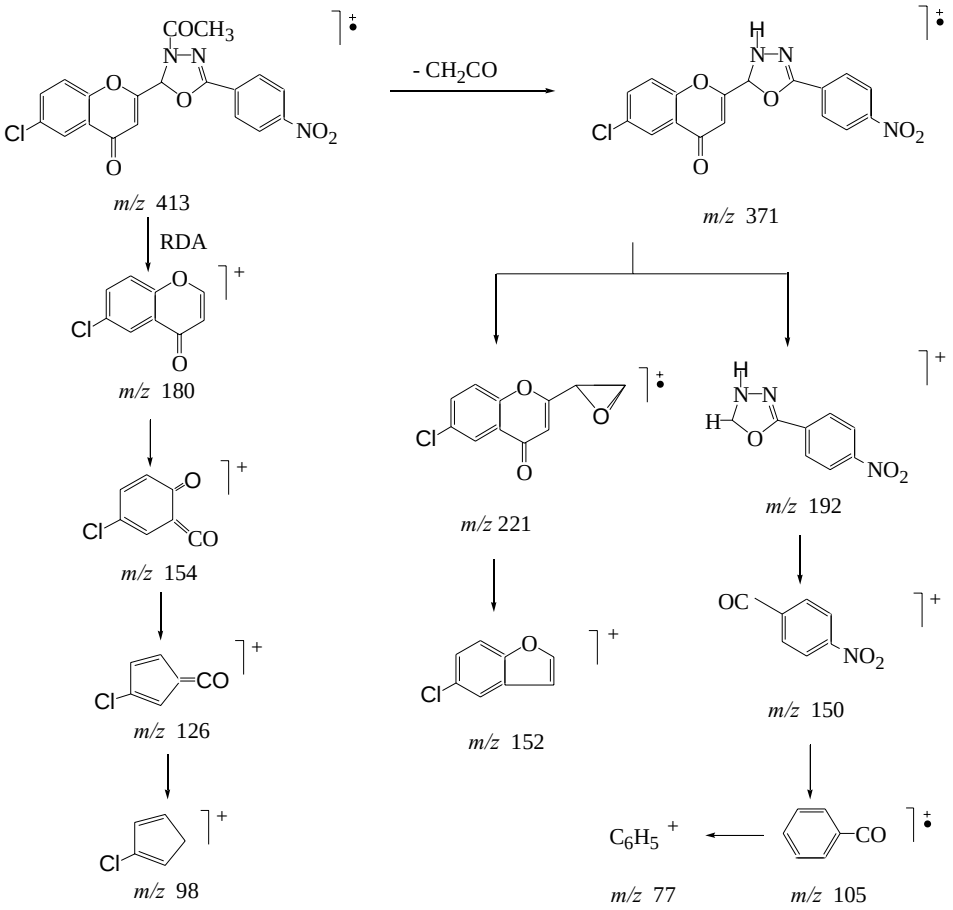
In EI-MS spectra, most of the compounds **22~41** have a molecular ion peak, but their abundance is less. This indicated compounds **22~41** were not very stable conjugate molecules. They also showed RDA fragmentation in which the flavone compounds were common. The compounds **22~41** were shown to lose CH_2=C=O at first, then formed 2-(1′,3′,4′-oxadiazole-2′-yl) chromones. Then they cleaved like oxadiazole type compounds. The cleaving of compounds **36** is in Scheme II. We confirmed the structure of those compounds by elemental analyses.

EXPERIMENTAL

General Method

Melting points were taken on a Yanaco MP-S3 micro melting point apparatus. The IR spectra were recorded in

Scheme II



KBr pellets on a Bruker FT-IR Equinox apparatus. The ^{1}H NMR spectra were recorded on an INOVA-400 (using TMS as internal standard, d_6-DMSO as solvent). MS were recorded on a HP 5890. Elemental analyses were performed on a Yanaco CHN Corder MT-3 analyzer. The TLC was performed by GF-254 and 0.5% CMC. Detection made use of UV light; the mobile phase was petroleum ether and ethyl acetate (1:1).

Preparation of 6-substituted 2-methyl chromones[6]

Under nitrogen atmosphere, the mixture of 0.2 mol 2-acetyl phenol and 165 mL ethyl acetate (free ethanol) was added dropwise into 8 g powdered sodium; when the vigorous reaction had ceased, the mixture was heated in an oil bath for an hour. The product was shaken with 150 g crushed ice. And the yellow sodium salt was filtered, washed with ice-cold water, then ether, and decomposed by treatment with 32% acetic acid. The crude product was filtered off as precipitate. 2-acetylacetyl phenol was recrystallized from ethanol.

2-acetylacetyl phenol (0.01 mol) was boiled for 2 min with acetic acid (10 mL), then a few drops of concentrated hydrochloric acid were added and refluxed for 15 min. After cooling, the mixture was poured into ice-water. The crude product was filtered off as precipitate and recrystallized from ethanol.

Preparation of 6-substituted 2-formyl chromones 1[11]

A solution of 6-substituted 2-methyl chromones (4 mmol) and *p*-nitrosodimethylaniline (12 mmol) in 10 mL ethanol (the least quantity) was added to an ethanolic solution of sodium ethoxide (4 mmol). After stirring, the red nitrones appeared, and were filtered off and recrystallized from n-butanol.

A mixture of nitrones (0.5 g) and 10 M sulphuric acid (8 mL) was shaken at room temperature for 15 min, and water (25 mL) was added to it. The crude products that were deposited were filtered off, washed with water and recrystallized from an appropriate solvent.

Preparation of 2-(Aroylhydrazonomethylidyne) Chromones 2~21

A solution of 6-substituted 2-formyl chromones **1** (0.5 g) in ethanol (15 mL) was added to a solution of an equimolar amount of aroylhydrazines in ethanol (5 mL) and 2 mL acetic acid as catalyst. After stirring for 15 min, precipitation appeared. Through TLC detection, the reaction was completed in 2 hours. The crude product was filtered and was recrystallized from DMF.

Preparation of 2-(3′-acetyl-5′-aryl-2′,3′-dihydro-1′,3′,4′-oxadiazol-2′-yl) Chromones 22~41

A mixture of aroylhydrazonomethylidyne chromone **2**~**21** (0.2 g) and acetic anhydride (50 mL) was refluxed for 3 h. After the reaction mixture was cooled, it was poured into ice-cold water. After excessive acetic anhydride was hydrolyzed, the solid was separated. It was recrystallized from ethanol.

22: Yield: 71%, m.p. 150-151 °C, $C_{19}H_{14}N_2O_4$, Calcd.: C, 68.26; H, 4.22; N, 8.38. Anal.: C, 68.41; H, 4.30; N, 8.43. δ_H: 8.21 (d × d, 1H, H-5, ^3J = 8.9 Hz, ^4J = 2.4 Hz), 7.78-7.52 (m, 3H, H-6, H-7, H-8), 7.49-7.31 (m, 3H, Ar-H), 7.30-7.28 (m, 2H, Ar-H), 7.15 (s, 1H, H-3), 6.73 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1680 (s, C=O), 1640 (s, pyrone C=O), 1604 (S-C=N), 1270 (m, C-O-C). *m/z* (%): 334 (M^+, 10), 292 (12), 187 (50), 146 (10), 120 (20), 105 (100), 92 (5), 77 (21).

23: Yield: 78%, m.p. 158-159 °C, $C_{19}H_{13}N_2O_4Cl$, Calcd.: C, 61.88; H, 3.55; N, 7.60. Anal.: C, 62.00; H, 3.58; N, 7.62. δ_H: 8.12 (m, 1H, H-5), 7.76-7.42 (m, 3H, H-6, H-7, H-8), 7.41-7.31 (m, 4H, Ar-H), 7.16 (s, 1H, H-3), 6.71 (s, 1H, oxadiazole-CH), 2.38 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1676 (s, C=O), 1648 (s, pyrone C=O), 1598 (s, C=N), 1275 (m, C-O-C). *m/z* (%): 368 (M^+, 10), 326 (12), 188 (20), 146 (16), 139 (100), 135 (10), 120 (19), 105 (32), 92 (5), 77 (18).

24: Yield: 76%, m.p. 160-161 °C, $C_{19}H_{13}N_2O_4Cl$, Calcd.: C, 61.88; H, 3.55; N, 7.60. Anal.: C, 61.89; H, 3.54; N, 7.62. δ_H: 8.12 (d × d, 1H, H-5, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.78-7.41 (m, 3H, H-6, H-7, H-8), 7.41-7.32 (m, 3H, Ar-H), 7.18-7.16 (m, 2H, H-3 & Ar-H), 6.72 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1680 (s, C=O), 1642 (s, pyrone C=O), 1596 (s, C=N), 1279 (m, C-O-C). *m/z* (%): 368 (M^+, 5), 326 (12), 188 (56), 139 (100), 120 (17), 105 (20), 92 (6), 77 (31).

25: Yield: 69%, m.p. 155-156 °C, $C_{20}H_{16}N_2O_5$, Calcd.: C, 65.93; H, 4.43; N, 7.69; Anal.: C, 66.00; H, 4.41; N, 7.67. δ_H: 7.99 (d × d, 1H, H-5, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.87-7.68 (m, 5H, H-6, H-7, H-8 & Ar-H), 7.68-7.67 (m, 2H, Ar-H), 7.13 (s, 1H, H-3), 6.73 (s, 1H, oxadiazole-CH), 3.84 (s, 3H, OCH_3), 2.38 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1678 (s, C=O), 1645 (s, pyrone C=O), 1598 (s, C=N), 1278 (m, C-O-C). *m/z* (%): 364 (M^+, 11), 322 (16), 188 (50), 177 (12), 146 (30), 135 (100), 117 (32), 120 (15), 105 (17), 92 (5), 77 (40).

26: Yield: 80%, m.p. 176-177 °C, $C_{19}H_{13}N_3O_6$, Calcd.: C, 60.16; H, 3.45; N, 11.08; Anal.: C, 59.60; H, 3.38; N, 11.49. δ_H: 8.40-8.38 (m, 4H, Ar-H), 8.14-8.13 (m, 3H, Ar-H), 7.97 (d × d, 1H, H-7, ^3J = 8.8 Hz, ^4J = 2.6 Hz), 7.12 (s, 1H, H-3), 6.72 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1680 (s, C=O), 1640 (s, pyrone C=O), 1590 (s, C=N), 1521 (m, -NO_2), 1347 (m, NO_2), 1273 (m, C-O-C). *m/z* (%): 379 (M^+, 9), 337 (15), 192 (6), 150 (100), 120 (19), 105 (28), 92 (5), 77 (20).

27: Yield: 70%, m.p. 203-204 °C, $C_{20}H_{16}N_2O_4$, Calcd.: C, 68.96; H, 4.63; N, 8.04; Anal.: C, 69.11; H, 4.59; N, 8.08. δ_H: 7.89-7.84 (m, 3H, 5-H, Ar-H), 7.64-7.51 (m, 5H, 7-H, 8-H, Ar-H), 7.14 (s, 1H, H-3), 6.73 (s, 1H, oxadiazole-CH), 2.42 (s, 3H, $COCH_3$), 2.32 (s, 3H, CH_3); IR (KBr) ν_{max} 1690-1664 (s, w, C=O & pyrone C=O), 1598 (m, C=N), 1286 (m, C-O-C). *m/z* (%): 348 (M^+, 7), 306 (7), 187 (25), 176 (2), 160 (7), 134 (28), 119 (19), 106 (5), 105 (100), 77 (19).

28: Yield: 74%, m.p. 175-176 °C, $C_{20}H_{15}N_2O_4Cl$, Calcd.: C, 62.75; H, 3.95; N, 7.32; Anal.: C, 62.98; H, 4.10; N, 7.28. δ_H: 7.92 (d, 1H, 5-H, ^4J = 2.4 Hz), 7.89-7.86 (m, 3H, H-7 & Ar-H), 7.72 (d, 1H, H-8, ^3J = 8.8 Hz), 7.64-7.55 (m, 2H, Ar-H), 7.17 (s, 1H, H-3), 6.83 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$), 2.32 (s, 3H, CH_3); IR (KBr) ν_{max} 1680 (s, C=O), 1645 (s, pyrone C=O), 1598 (m, C=N), 1280 (m, C-O-C). *m/z* (%): 382 (M^+, 6), 340 (10), 210 (50), 201 (28), 160 (5), 139 (100), 134 (26), 119(17), 115 (20), 106 (5), 77 (22).

29: Yield: 72%, m.p. 184-185 °C, $C_{20}H_{15}N_2O_4Cl$, Calcd.: C, 62.75; H, 3.95; N, 7.32; Anal.: C, 63.01; H, 4.11; N, 7.18. δ_H: 7.91 (d, 1H, 5-H, ^4J = 2.4 Hz), 7.88-7.86 (m, 3H, H-7, Ar-H), 7.72 (d, 1H, H-8, ^3J = 8.8 Hz), 7.63-7.55 (m, 2H, Ar-H), 7.16 (s, 1H, H-3), 6.83 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$), 2.32 (s, 3H, CH_3); IR (KBr) ν_{max} 1678-1648 (s, C=O & pyrone C=O), 1598 (m, C=N), 1282 (m, C-O-C), 1378 (m, -CH_3). *m/z* (%): 382 (M^+, 5), 340 (12), 210 (50), 201 (26), 160 (6), 139 (100), 134 (26), 119 (18), 115 (21), 106 (5), 77 (19).

30: Yield: 64%, m.p. 150-151 °C, $C_{21}H_{18}N_2O_5$, Calcd.: C, 65.57; H, 4.95; N, 7.65. Anal.: C, 65.48; H, 4.91; N, 7.69. δ_H: 7.99 (d, 1H, 5-H, ^4J = 2.6 Hz), 7.89-7.87 (m, 3H, H-7 & Ar-H), 7.72 (d, 1H, H-8, ^3J = 9.2 Hz), 7.63-7.55 (m, 2H, Ar-H), 7.16 (s, 1H, H-3), 6.83 (s, 1H, oxadiazole-CH), 3.57 (s, 3H, OCH_3), 2.39 (s, 3H, $COCH_3$), 2.32 (s, 3H, CH_3). IR (KBr) ν_{max} 1681 (s, C=O), 1640 (s, pyrone C=O), 1590 (m, C=N), 1280 (C-O-C). *m/z* (%): 378 (M^+, 8), 336 (10), 201

(25), 206 (16), 135 (100), 160 (5), 134 (26), 119 (21), 106 (4), 77 (19).

31: Yield: 78%, m.p. 168-169 °C, $C_{20}H_{15}N_3O_6$, Calcd.: C, 61.07; H, 3.84; N, 10.68. Anal.: C, 61.48; H, 3.76; N, 10.40. δ_H: 8.40-8.37 (m, 2H, Ar-H), 8.13-8.11 (m, 3H, H-5, Ar-H), 7.98 (d×d, 1H, H-7, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.82 (d, 1H, H-8, ^3J = 8.8 Hz), 7.23 (s, 1H, H-3), 6.89 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$), 2.32 (s, 3H, CH_3). IR (KBr) ν_{max} 1685 (s, C=O), 1640 (s, pyrone C=O), 1598 (m, C=N), 1521 (m, NO_2), 1347 (m, -NO_2), 1280 (m, C-O-C). *m/z* (%): 393 (5), 350 (7), 201 (25), 160 (5),150 (100), 134 (27), 119 (15), 106 (7), 104 (21), 77 (19).

32: Yield: 76%, m.p. 165-166 °C, $C_{19}H_{13}N_2O_4Cl$, Calcd.: C, 61.88; H, 3.55; N, 7.60. Anal.: C, 62.10; H, 3.49; N, 7.72. δ_H: 8.11 (d, 1H, H-5, ^4J = 2.4 Hz), 7.96 (d × d, 1H, H-7, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.82-7.82 (m, 3H, Ar-H), 7.63 (d, 1H, H-8, ^3J = 8.8 Hz), 7.09-7.00 (m, 3H, H-3 & Ar-H), 6.88 (s, 1H, oxadiazole-CH), 2.39 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1682 (s, C=O), 1645 (s, pyrone C=O), 1598 (m, C=N), 1210 (m, C-O-C). *m/z* (%): 326 (18), 221 (54), 180 (9), 154 (32), 139 (6), 126 (10), 105 (100), 98 (7), 77 (10).

33: Yield: 74%, m.p. 168-169 °C, $C_{19}H_{12}N_2O_4Cl_2$, Calcd.: C, 56.60; H, 3.00; N, 6.95; Anal.: C, 56.54; H, 3.02; N, 6.94. δ_H: 7.99 (d, 1H, H-5, ^4J = 2.8 Hz), 7.89-7.86 (m, 3H, H-7 & Ar-H), 7.72 (d, 1H, H-8, ^3J = 9.2 Hz), 7.64-7.55 (m, 2H, Ar-H), 7.17 (s, 1H, H-3), 6.87 (s, 1H, oxadiazole-CH), 2.32 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1680-1644 (s, C=O & pyrone C=O), 1604 (s, C=N), 1259 (m, C-O-C), 621(v, C-Cl). *m/z* (%): 361 (18), 221 (50), 180 (10), 154 (6), 139 (100), 126 (10), 115 (34), 98 (8), 77 (20).

34: Yield: 70%, m.p. 166-167 °C, $C_{19}H_{12}N_2O_4Cl_2$, Calcd.: C, 56.60; H, 3.00; N, 6.95; Anal.: C, 56.55 ; H, 3.01; N, 7.01. δ_H: 7.99 (d, 1H, H-5, ^4J = 2.8 Hz), 7.88-7.86 (m, 3H, H-7 & Ar-H), 7.72 (d, 1H, H-8, ^3J = 9.2 Hz), 7.63-7.55 (m, 2H, Ar-H), 7.16 (s, 1H, H-3), 6.82 (s, 1H, oxadiazole-CH), 2.32 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1682 (s, C=O), 1645 (s, pyrone C=O), 1596 (s, C=N), 1268 (m, C-O-C). *m/z* (%): 361 (19), 221 (50), 180 (10), 154 (8), 139 (100), 126 (11), 98 (8), 77 (26).

35: Yield: 72%, m.p. 162-163 °C, $C_{20}H_{15}N_2O_5Cl$, Calcd.: C, 60.24; H, 3.79; N, 7.02; Anal.: C, 60.30; H, 3.81; N, 7.05. δ_H: 7.99 (d, 1H, H-5, ^4J = 2.81 Hz), 7.87-7.80 (m, 3H, H-7 & Ar-H), 7.77 (d, 1H, H-8, ^3J = 8.8 Hz), 7.12-7.09 (m, 3H, Ar-H), 6.80 (s, 1H, oxadiazole-CH), 3.84 (s, 3H, OCH_3), 2.34 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1680 (s, C=O), 1645 (s, pyrone C=O), 1598 (s, C=N), 1280 (m, C-O-C). *m/z* (%): 356 (19), 221 (51), 154 (6), 135 (100), 139 (8), 140 (60), 126 (10), 98 (7), 77 (20).

36: Yield: 81%, m.p. 201-202 °C, $C_{19}H_{12}N_3O_6Cl$, Calcd.: C, 55.15; H, 2.92; N, 10.16; Anal.: C, 55.00; H, 2.90; N, 10.19. δ_H: 8.40-8.38 (m, 2H, Ar-H), 8.13-8.11 (m, 3H, H-5 & Ar-H), 7.97 (d × d, 1H, H-7, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.65 (1H, d, H-8, ^3J = 8.8 Hz), 7.22 (s, 1H, H-3), 6.88 (s, 1H, oxadiazole-CH), 2.34 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1681 (s, C=O), 1663 (s, pyrone C=O), 1598 (m, C=N), 1521, 1347 (m, NO_2), 1273 (C-O-C). *m/z* (%): 413 (M^+, 3), 371 (17), 221 (53), 154 (5), 150 (100), 139 (7), 126 (11), 104 (34), 98 (8), 77 (22).

37: Yield: 70%, m.p. 172-173 °C, $C_{19}H_{13}N_2O_4Br$, Calcd.: C, 55.23; H, 3.17; N, 6.78; Anal.: C, 55.28; H, 3.19; N, 6.81. δ_H: 8.11 (d, 1H, H-5, ^4J = 2.4 Hz), 7.96 (d × d, 1H, H-7, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.81 (m, 3H, Ar-H), 7.63 (d, 1H, H-8, ^3J = 8.8 Hz), 7.08-7.72 (m, 3H, H-3), 6.79 (s, 1H, oxadiazole-CH), 2.29 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1685 (s, C=O), 1643 (s, pyrone C=O), 1598 (s, C=N), 1283 (m, C-O-C). *m/z* (%): 412 (M^+, 3), 370 (8), 307 (2), 265 (12), 225 (4), 199 (6), 196 (15), 171 (7), 143 (5), 105 (100), 77 (30).

38: Yield: 76%, m.p. 149-150 °C, $C_{19}H_{12}N_2O_4BrCl$, Calcd.: C, 50.98; H, 2.70; N, 6.26; Anal.: C, 51.00; H, 2.72; N, 6.29. δ_H: 8.10 (d, 1H, H-5, ^4J = 2.4 Hz), 7.96 (d×d, 1H, H-7, ^3J = 8.8 Hz, ^4J = 2.4 Hz), 7.81 (m, 3H, Ar-H), 7.62 (d, 1H, H-8, ^3J = 8.8 Hz), 7.72-7.08 (m, 2H, Ar-H), 6.79 (s, 1H, oxadiazole-CH), 2.32 (s, 1H, $COCH_3$). IR (KBr) ν_{max} 1690 (s, C=O), 1660 (s, pyrone C=O), 1602 (m, C=N), 1270 (m, C-O-C), 804 (m, C-Cl), 612 (v, C-Br). *m/z* (%): 446 (M^+, 3), 402 (4), 265 (6), 225 (5), 210 (12), 199 (8), 171 (6), 143 (5), 139 (100), 104 (30), 77 (20).

39: Yield: 70%, m.p. 152-153 °C, $C_{19}H_{12}N_2O_4BrCl$, Calcd.: C, 50.98; H, 2.70; N, 6.26; Anal.: C, 51.01; H, 2.73; N, 6.25. δ_H: 7.98 (d, 1H, H-5, ^4J = 2.8 Hz), 7.88-7.86 (m, 3H, H-7 & Ar-H), 7.72 (d, 1H, H-8, ^3J = 9.2 Hz), 7.64-7.55 (m, 2H, Ar-H), 7.16 (s, 1H, H-3), 6.82 (s, 1H, oxadiazole-CH), 2.32 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1690 (s, C=O), 1663 (s, pyrone C=O), 1602 (m, C=N), 1272 (m, C-O-C), 803 (m, C-Cl), 611 (v, C-Br). *m/z* (%): 446 (M^+, 3), 402 (2), 265 (8), 225 (5), 210 (14), 199 (5), 184 (9), 171 (6), 143 (5), 139 (100), 104 (28), 77 (20).

40: Yield: 70%, m.p. 159-160 °C, $C_{20}H_{15}N_2O_5Br$, Calcd.: C, 54.19; H, 3.41; N, 6.32; Anal.: C, 54.20; H, 3.43; N, 6.30. δ_H: 8.11 (d, 1H, H-5, ^4J = 2.4 Hz), 7.96 (d × d, 1H, H-7, ^3J = 9 Hz, ^4J = 2.8 Hz), 7.88-7.86 [m, 2H, Ar-H (*o*-OCH_3)], 7.65-7.54 (m, 3H, H-8 & Ar-H), 7.16 (s, 1H, H-3), 6.82 (s, 1H, oxadiazole-CH), 3.51 (s, 1H, OCH_3), 2.32 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1690 (s, C=O), 1660 (s, pyrone C=O), 1598 (m, C=N), 1280 (m, C-O-C), 612 (v, C-Br). *m/z* (%): 401 (4), 265 (21), 225 (4), 204 (8), 199 (7), 184 (6), 171 (6), 143 (5), 135 (100), 104 (36), 77 (28).

41: Yield: 80%, m.p. 198-199 °C, $C_{19}H_{12}N_3O_6Br$,

Calcd.: C, 49.80; H, 2.64; N, 9.17; Anal.: C, 49.91; H, 2.66; N, 9.21. δ_H: 8.40-8.37 [m, 2H, Ar-H (*o*-NO_2)], 8.13-8.11 [m, 3H, H-5 & Ar-H (*m*-NO_2)], 7.97 (d × d, 1H, H-7, ^3J = 8.2 Hz, ^4J = 2.4 Hz), 7.65 (d, 1H, ^3J = 8.8 Hz), 7.22 (s, 1H, H-3), 6.88 (s, 1H, oxadiazole-CH), 2.34 (s, 3H, $COCH_3$). IR (KBr) ν_{max} 1690 (s, C=O), 1663 (s, pyrone C=O), 1598 (s, C=N), 1521 (m, NO_2), 1347 (s, -NO_2), 1272 (s, C-O-C), 611 (v, C-Br). *m/z* (%): 265 (20), 225 (4), 199 (6), 184 (9), 171 (6), 143 (5), 150 (100), 104 (28), 77 (29).

ACKNOWLEDGEMENT

This work was supported by the Natural Science Foundation of the PRC (Grant No. 29962002) and Nankai University State Key Laboratory of Elemento-Organic Chemistry.

Received August 16, 2002.

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