Chemistry of Natural Compounds, Vol. 45, No. 3, 2009

7-HYDROXY-3-PHENOXY-8-FORMYLCHROMONES, ANALOGS OF NATURAL FLAVONOIDS

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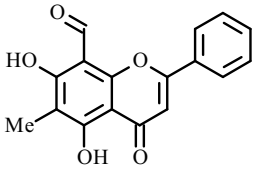
7-Hydroxy-3-phenoxy-8-formylchromones were synthesized using the Duff reaction and were reacted with 2,4-dinitrophenylhydrazine to produce hydrazones and with an excess of hydrazine hydrate to produce the pyrazole recyclization products. Derivatives of α-pyrono[2,3-f]chromones were synthesized using the Knoevenagel condensation with 2-azahetarylacetonitriles and the Perkin reaction.

Key words: 7-hydroxy-8-formylchromones, condensation, α-pyrono[2,3-f]chromones.

Few 7-hydroxy-8-formylchromones (isounonal **1**) and their partially hydrogenated derivatives, lavinal (**2**), and 4,7-dihydroxy-6-methyl-5-methoxy-8-formylflavan (**3**) have been discovered within the broad class of natural flavonoids.



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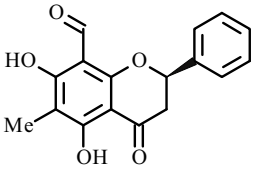

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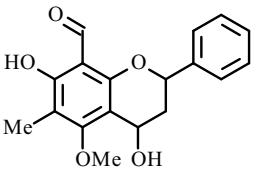

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The first two occur together in plants of the family Annonaceae [1-6] such as *Dasymaschalon rostratum* [1], *Desmos chinensis* Lour [2], *Desmos cochinchinensis* [3], and *Unona lawii* Hook. f. & Thoms [4]. The last is found in roots of *Desmos cochinchinensis* [3]. A mixture of all three flavonoids isolated from *D. cochinchinensis* [3] exhibited antimalarial activity whereas lavinal itself was viewed as a potential AIDS agent [7]. Phenoxychromones are also found in nature [8]. This enabled us to combine these two classes into one in order to study properties different from those of each class individually but characteristic of the system as a whole.

The classical method for synthesizing 7-hydroxy-8-formylchromones is the Duff reaction [9-15]. Starting 7-hydroxy-3-phenoxy-8-formylchromones **4**-**10** were synthesized using the Duff reaction by heating chromones **11**-**17** with urotropine in acetic acid with subsequent work up of the reaction mixture by HCl solution. PMR spectra of these compounds in DMSO-d_6 showed a singlet for the formyl group near 10.5 ppm and a broad singlet for the hydroxyl proton that was shifted to weak field relative to the resonance of the hydroxyl in the starting chromone by 1.6-1.7 ppm as a result of the formation of an intramolecular H-bond.

The presence of the formyl group was also confirmed by formation of the 2,4-dinitrophenylhydrazone **18** upon reaction of **8** with 2,4-dinitrophenylhydrazine. The PMR spectrum of **18** exhibited resonances for aromatic protons characteristic of starting chromone **8**; 1H doublets for H-5″ and H-6″ at 8.39 and 7.89 ppm, respectively; and a singlet for H-3″ of the 2,4-dinitrophenyl group at 8.90 ppm.

The reaction of 8-formylchromone **6** with an excess of hydrazine hydrate did not stop at the formation of the hydrazone but led to recyclization of the γ-pyrone ring to form pyrazole **19**. This was confirmed by a broad singlet typical of the pyrazole NH proton at 12.90 ppm, singlets for two hydroxyls at 11.78 and 12.07, and a 2H singlet at 6.69 for the hydrazone amino group in the PMR spectrum recorded in DMSO-d_6.

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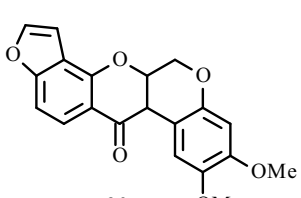

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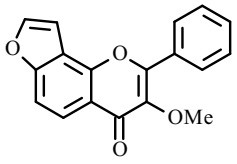

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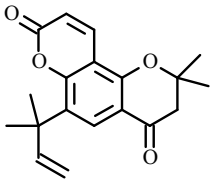

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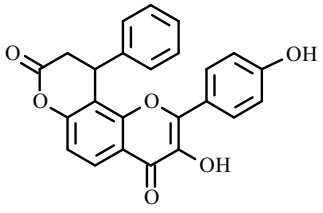

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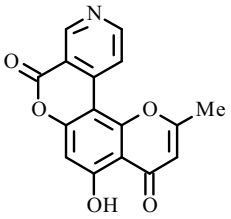

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The hydroxyl located in the position *ortho* to the carbonyl provides several possibilities for annelating *O*-containing heterocycles to the chromone system. The furo[2,3-*h*]chromone system is the basis of naturally occurring elliptone (**20**) [9, 10] and caraniine (**21**) [12, 13]. The α-pyrono[2,3-*f*]chromone core is found in clausenidin (**22**) [16, 17], calomelanol D (**23**) [18], and schumanniophytine (**24**) [19, 20].

The synthesis of compounds similar to angular α-pyrono[2,3-*f*]chromones is promising because they are active against *S. aureus* and *E. coli* [21, 22]. Derivatives of this system were synthesized previously starting with 7-hydroxy-8-formylchromones using the Perkin [11, 23, 24] and Knoevenagel [24, 25] reactions. We used both methods to synthesize 3-phenoxy derivatives of this system. 2-Methyl-3-(4-chlorophenoxy)pyrano[2,3-*f*]chromen-4,8-dione (**25**) was prepared via reaction of 7-hydroxy-8-formylchromone (**5**) with acetic anhydride and sodium acetate. The PMR spectrum of **25** showed doublets at 6.97 and 8.72 ppm due to splitting of vicinal protons H-9 and H-10 of the α-pyrone ring. The doublet for H-10 at 8.72 shifted to weaker field, which was characteristic for a system of conjugated vinyl and carbonyl groups and occurred in α,β-unsaturated carbonyl compounds. A strong band for lactone carbonyl at 1745 cm^{-1} in the IR spectrum was indicative of an α-pyrone ring.

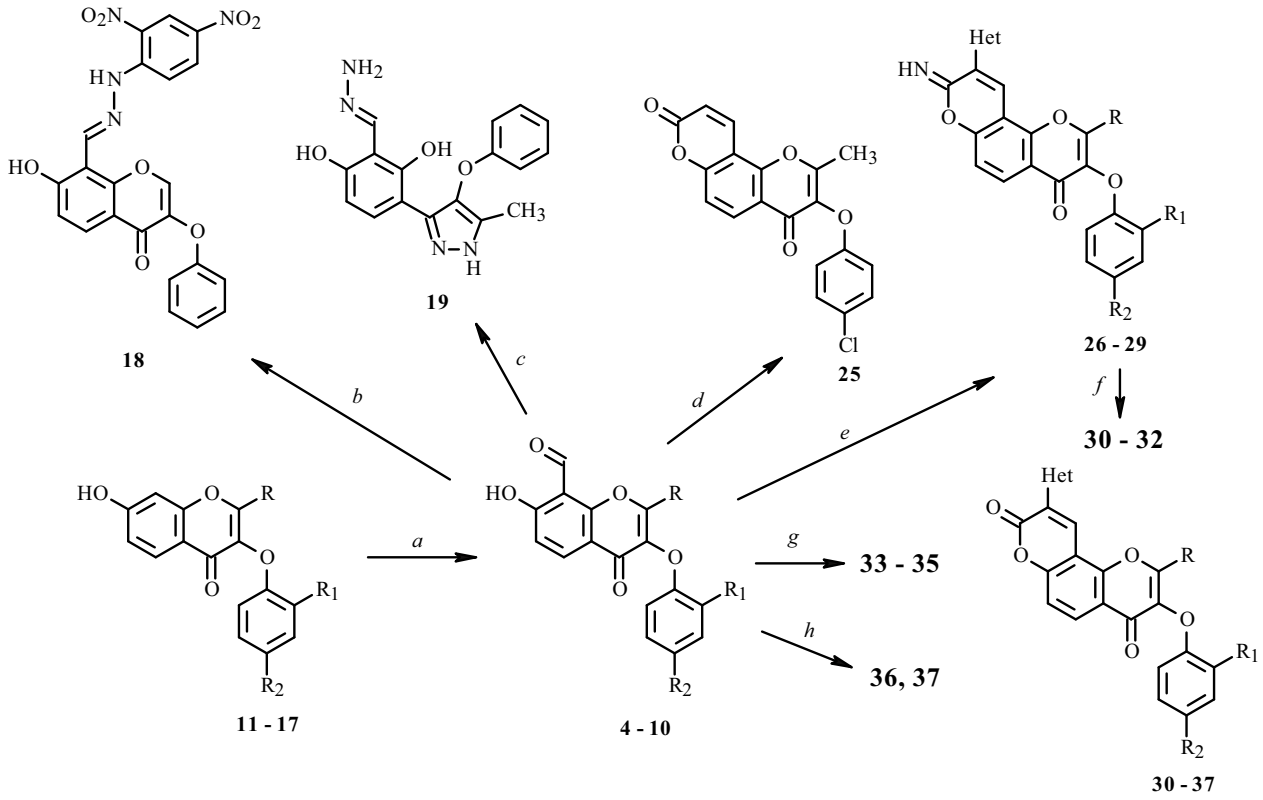
The reaction of 7-hydroxy-3-phenoxy-8-formylchromones **4**, **5**, and **8** with 2-azolylacetonitriles was carried out in propan-2-ol with basic catalysis by piperidine. Intermediates 9-azolyl-8-imino-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-ones **26**-**29** could be isolated under these conditions. The structures of the isolated intermediates **26**-**29** were confirmed by the presence in the IR spectra of NH stretching bands at 3330-3285 cm^{-1} and a strong-field singlet for H-10 in the α-pyrone ring at 9.34-9.56 ppm in the PMR spectra recorded in CF_3CO_2D. Hydrolysis of **26**-**29** to the corresponding 9-hetaryl-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-diones **30**-**32** was carried out in acetic acid or its mixture with HCl.

Pure imines could not be isolated from the reaction of **5**, **8**, and **9** with 2-azinylacetonitriles and 4-(benzodioxol-5-yl)thiazol-2-ylacetonitrile because of their partial hydrolysis. In this instance the mixture was hydrolyzed to the corresponding diones **33**-**35**, analogously to **26**-**29**.

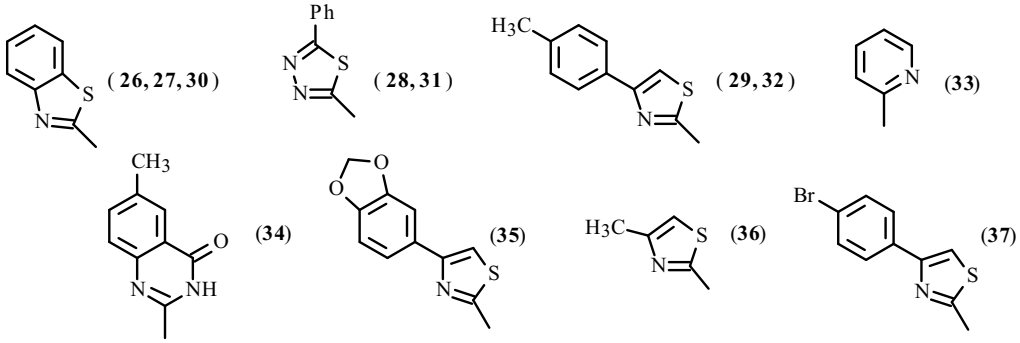
The Knoevenagel reaction was performed in DMF with addition of catalytic amounts of piperidine and subsequent hydrolysis by H_2SO_4 (3%) because of the poor solubility of 8-formylchromones **7** and **9** in propan-2-ol. This produced the corresponding α-pyrono[2,3-*f*]chromones **36** and **37** in a one-flask method.

The weak-field shift of the resonance for H-10 by 0.4-0.5 ppm relative to the corresponding resonance of imino derivatives **26**-**29** in PMR spectra recorded in CF_3CO_2D and the presence of stretching vibrations of an γ-pyrone ring at 1660-1640 cm^{-1} and an α-pyrone ring at 1745-1725 cm^{-1} in the IR spectra proved the structures of products **30**-**37**.

Thus, previously unknown 7-hydroxy-3-phenoxy-8-formylchromones were synthesized. Their reactivity toward hydrazines was investigated. An α-pyrone ring was added to the chromone core using the Knoevenagel and Perkin reactions.



4, 11: R = CH_3, R_1 = H, R_2 = CO_2CH_3; **5, 12:** R = CH_3, R_1 = H, R_2 = Cl; **6, 13:** R = CH_3, R_1 = R_2 = H
7, 14: R = R_2 = H, R_1 = OCH_3; **8, 15:** R = R_1 = R_2 = H; **9, 16:** R = R_1 = H, R_2 = F; **10, 17:** R = CF_3, R_1 = R_2 = H
26: R = CH_3, R_1 = H, R_2 = CO_2CH_3; **27, 30:** R = CH_3, R_1 = H, R_2 = Cl; **28, 31:** R = CH_3, R_1 = H, R_2 = Cl
29, 32: R = R_1 = R_2 = H; **33:** R = CH_3, R_1 = H, R_2 = Cl; **34:** R = R_1 = H, R_2 = F; **35:** R = R_1 = R_2 = H
36: R = R_1 = H, R_2 = F; **37:** R = H, R_1 = OCH_3, R_2 = H

Het:  (**26, 27, 30**) (**28, 31**) (**29, 32**) (**33**) (**34**) (**35**) (**36**) (**37**)

a. $(CH_2)_6N_4$, AcOH; *b*. $H_2NNHC_6H_3(NO_2)_2$; *c.* $N_2H_4 \cdot H_2O$; *d*. NaOAc, Ac_2O; *e*. $HetCH_2CN$, *i*-PrOH, pip; *f.* AcOH, HCl
g. 1. $HetCH_2CN$, *i*-PrOH, pip, 2. AcOH, HCl; *h*. 1. $HetCH_2CN$, DMF, pip, 2. 3% H_2SO_4

EXPERIMENTAL

The purity of products was monitored by TLC on Silufol UV-254 plates with elution by $CHCl_3$:CH_3OH (9:1). PMR spectra in DMSO-d_6 and CF_3CO_2D were recorded on a Varian Mercury 400 spectrometer relative to TMS (internal standard); IR spectra in KBr disks, on a UR-20 instrument. Elemental analyses of all compounds agreed with those calculated.

General Method for Synthesizing 7-Hydroxy-3-phenoxy-8-formylchromones 4-10. 7-Hydroxy-3-phenoxychromone (**11-17**, 5 mmol) and hexamethylenetetramine (4.9 g, 35 mmol) in glacial acetic acid (20 mL) were heated

for 6 h on a water bath, poured into a mixture (20 mL) of HCl and water (1:1), cooled, treated in portions with water (40 mL), and left overnight. The resulting precipitate was filtered off, washed with water, and recrystallized as necessary from an appropriate solvent.

7-Hydroxy-2-methyl-3-(4-methoxycarbonyl)-8-formylchromone (4). Yield 58%, mp 182°C, $C_{19}H_{14}O_7$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.45 (3H, s, CH_3-2), 3.84 (3H, s, CO_2CH_3), 7.01 (2H, d, J = 8.8, H-2′, H-6′), 7.07 (1H, d, J = 9.2, H-6), 7.90 (2H, d, J = 8.8, H-3′, H-5′), 8.15 (1H, d, J = 9.2, H-5), 10.58 (1H, s, CHO-8), 12.27 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1640 (C=O), 1705 (C=Oest).

7-Hydroxy-2-methyl-8-formyl-3-(4-chlorophenoxy)chromone (5). Yield 73%, mp 182°C (MeOH), $C_{17}H_{11}ClO_5$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.45 (3H, s, CH_3-2), 6.94 (2H, d, J = 8.8, H-2′, H-6′), 7.05 (1H, d, J = 9.2, H-6), 7.26 (2H, d, J = 8.8, H-3′, H-5′), 8.15 (1H, d, J = 9.2, H-5), 10.58 (1H, s, CHO-8), 12.54 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1640 (C=O).

7-Hydroxy-2-methyl-3-phenoxy-8-formylchromone (6). Yield 56%, mp 150°C, $C_{17}H_{12}O_5$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.44 (3H, s, CH_3-2), 6.90 (2H, d, J = 8.0, H-2′, H-6′), 7.00 (1H, t, J = 8.0, H-4′), 7.05 (1H, d, J = 9.2, H-6), 7.26 (2H, t, J = 8.0, H-3′, H-5′), 8.14 (1H, d, J = 9.2, H-5), 10.57 (1H, s, CHO-8), 12.25 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1640 (C=O).

7-Hydroxy-3-(2-methoxyphenoxy)-8-formylchromone (7). Yield 49%, mp 125°C, $C_{17}H_{12}O_6$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.86 (3H, s, CH_3O-2′), 6.83-7.03 (4H, m, H-3′, H-4′, H-5′, H-6′), 7.08 (1H, d, J = 9.2, H-6), 8.22 (1H, d, J = 9.2, H-5), 8.26 (1H, s, H-2), 10.51 (1H, s, CHO-8), 12.92 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1650, 1640 (C=O).

7-Hydroxy-3-phenoxy-8-formylchromone (8). Yield 50%, mp 130°C, $C_{16}H_{10}O_5$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.96 (2H, d, J = 8.0, H-2′, H-6′), 7.03 (1H, t, J = 8.0, H-4′), 7.09 (1H, d, J = 9.2, H-6), 7.29 (2H, t, J = 8.0, H-3′, H-5′), 8.21 (1H, d, J = 9.2, H-5), 8.54 (1H, s, H-2), 10.54 (1H, s, CHO-8), 12.28 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1660, 1640 (C=O).

7-Hydroxy-8-formyl-3-(4-fluorophenoxy)chromone (9). Yield 53%, mp 146°C (*i*-PrOH), $C_{16}H_9FO_5$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.90-7.06 (4H, m, H-2′, H-3′, H-5′, H-6′), 7.09 (1H, d, J = 9.2, H-6), 8.19 (1H, d, J = 9.2, H-5), 8.56 (1H, s, H-2), 10.53 (1H, s, CHO-8), 12.29 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1645 (C=O).

7-Hydroxy-3-phenoxy-8-formyl-2-trifluoromethylchromone (10). Yield 39%, mp 156°C, $C_{17}H_9F_3O_5$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.01 (2H, d, J = 8.0, H-2′, H-6′), 7.08 (1H, t, J = 8.0, H-4′), 7.17 (1H, d, J = 8.8, H-6), 7.30 (2H, t, J = 8.0, H-3′, H-5′), 8.15 (1H, d, J = 8.8, H-5), 10.51 (1H, s, CHO-8), 12.37 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 1664, 1650 (C=O).

7-Hydroxy-4-oxo-3-phenoxy-4*H*-chromen-8-carbaldehyde 2,4-Dinitrophenylhydrazone (18). A solution of **8** (0.17 g, 0.6 mmol) in EtOH (10 mL) was treated with 2,4-dinitrophenylhydrazine (0.12 g, 0.6 mmol), heated until dissolved, and left at room temperature for 12 h. The precipitate was filtered off and washed with EtOH and Et_2O. Yield 50%, mp 138°C, $C_{22}H_{14}N_4O_8$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.98 (2H, d, J = 7.6, H-2′, H-6′), 7.03 (1H, t, J = 7.6, H-4′), 7.08 (1H, d, J = 8.8, H-6), 7.29 (2H, t, J = 7.6, H-3′, H-5′), 7.89 (1H, d, J = 9.2, H-6″), 8.00 (1H, d, J = 8.8, H-5), 8.39 (1H, d, J = 9.2, H-5″), 8.70 (1H, s, H-2), 8.90 (1H, s, H-3″), 9.28 (1H, s, H-9), 11.54 (1H, s, NH), 11.92 (1H, s, OH-7). IR spectrum (KBr, ν, cm^{-1}): 3400 (NH_{as}), 3290 (NH_s), 1660 ($C=O_\gamma$).

2,6-Dihydroxy-3-(5-methyl-4-phenoxy-1*H*-pyrazol-3-yl)benzaldehyde Hydrazone (19). A solution of **6** (0.29 g, 1 mmol) in EtOH (10 mL) was treated with hydrazine hydrate (0.1 g, 3 mmol), heated for 15 min until the solid dissolved, and cooled. The precipitate was filtered off and washed with EtOH. Yield 49%, mp 280°C, $C_{12}H_{16}N_4O_3$. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.09 (3H, s, CH_3-3), 6.16 (1H, d, J = 8.0, H-5), 6.69 (2H, s, NH_2), 6.89 (2H, d, J = 8.0, H-2′, H-6′), 6.98 (1H, t, J = 8.0, H-4′), 7.27 (2H, t, J = 8.0, H-3′, H-5′), 7.38 (1H, d, J = 8.0, H-6), 8.33 (1H, s, CH=N), 11.78 (1H, s, OH-4), 12.07 (1H, s, OH-2), 12.90 (1H, br.s, NH). IR spectrum (KBr, ν, cm^{-1}): 3400 (NH_{as}), 3290 (NH_s).

2-Methyl-3-(4-chlorophenoxy)-4*H*,8*H*-pyrano-2,3-*f*-chromen-4,8-dione (25). A solution of **5** (0.33 g, 1 mmol) in acetic anhydride (10 mL, 0.1 mol) was treated with sodium acetate (1 g, 12 mmol), heated for 6 h on an oil bath at 175-180°C, and poured into water (30 mL). The resulting precipitate was filtered off after two days. Yield 85%, mp 214°C (AcOH), $C_{19}H_{11}ClO_5$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.19 (3H, s, CH_3-2), 6.94 (2H, d, J = 8.8, H-2′, H-6′), 6.97 (1H, d, J = 9.6, H-9), 7.33 (2H, t, J = 8.8, H-3′, H-5′), 7.69 (1H, d, J = 9.2, H-6), 8.63 (1H, d, J = 9.2, H-5), 8.72 (1H, d, J = 9.6, H-10). IR spectrum (KBr, ν, cm^{-1}): 1745 ($C=O_\alpha$), 1650 ($C=O_\gamma$).

General Method for Synthesizing 9-Hetaryl-8-imino-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-ones 26-29. A solution of 7-hydroxy-8-formyl-3-phenoxychromone **4**, **5**, or **8** (2 mmol) in *i*-PrOH (30 mL) was treated with 2-hetarylacetonitrile (2 mmol) and three drops of piperidine and held at room temperature for 12 h. The precipitate was filtered off and washed with MeOH and Et_2O.

9-(Benzthiazol-2-yl)-8-imino-2-methyl-3-(4-methoxycarbonylphenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-one (26). Yield 59%, mp 267°C (DMF), $C_{28}H_{18}N_2O_6S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.78 (3H, s, CH_3-2), 4.09 (3H, s, CO_2CH_3), 7.13 (2H, d, J = 8.8, H-2′, H-6′), 7.71 (1H, t, J = 8.0, H-6″), 7.76 (1H, t, J = 8.0, H-5″), 7.92 (1H, d, J = 8.8, H-6), 8.11 (1H, d, J = 8.0, H-4″), 8.16 (2H, d, J = 8.8, H-3′, H-5′), 8.25 (1H, d, J = 8.0, H-7″), 8.89 (1H, d, J = 8.8, H-5), 9.47 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1640 ($C{=}O_\gamma$), 1705 (C=O), 3285 (NH).

9-(Benzthiazol-2-yl)-8-imino-2-methyl-3-(4-chlorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-one (27). Yield 69%, mp 284°C (DMF), $C_{26}H_{15}ClN_2O_4S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.76 (3H, s, CH_3-2), 6.93 (2H, d, J = 8.8, H-2′, H-6′), 7.32 (2H, d, J = 8.8, H-3′, H-5′), 7.70 (1H, t, J = 8.0, H-6′), 7.75 (1H, t, J = 8.0, H-5″), 7.89 (1H, d, J = 9.2, H-6), 8.09 (1H, d, J = 8.0, H-4″), 8.24 (1H, d, J = 8.0, H-7″), 8.88 (1H, d, J = 9.2, H-5), 9.46 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1640 ($C{=}O_\gamma$), 3310 (NH).

8-Imino-2-methyl-9-(5-phenyl-1,3,4-thiadiazol-2-yl)-3-(4-chlorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-one (28). Yield 80%, mp 278°C (*i*-PrOH), $C_{27}H_{16}ClN_3O_4S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.75 (3H, s, CH_3-2), 6.94 (2H, d, J = 8.8, H-2′, H-6′), 7.33 (2H, d, J = 8.8, H-3′, H-5′), 7.72 (2H, t, J = 7.6, H-3″, H-5″), 7.80 (1H, t, J = 7.6, H-4″), 7.94 (1H, d, J = 9.2, H-6), 8.09 (2H, d, J = 7.6, H-2″, H-6″), 8.96 (1H, d, J = 9.2, H-5), 9.56 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1640 ($C{=}O_\gamma$), 3320 (NH).

8-Imino-9-[4-(4-methylphenyl)-1,3-thiazol-2-yl]-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-one (29). Yield 59%, mp 248°C (DMF), $C_{28}H_{18}N_2O_4S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.43 (3H, s, CH_3-4‴), 7.14 (2H, d, J = 7.6, H-2′, H-6′), 7.28 (1H, t, J = 7.6, H-4′), 7.35 (2H, d, J = 7.6, H-3″, H-5‴), 7.46 (2H, t, J = 7.6, H-3′, H-5′), 7.77 (2H, d, J = 7.6, H-2‴, H-6‴), 7.88 (1H, d, J = 9.2, H-6), 7.89 (1H, s, H-5″$_{Th}$), 8.34 (1H, s, H-2), 8.93 (1H, d, J = 9.2, H-5), 9.34 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1650 ($C{=}O_\gamma$), 3330 (NH).

General Method for Synthesizing 9-Hetaryl-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-diones 30-37.

Method A. Pure 9-hetaryl-8-imino-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4-one (**21**-**24**, 1 mmol) or partially hydrolyzed product was refluxed in AcOH (2 mL) or in AcOH (1 mL) and HCl (2 mL) with stirring and held at room temperature for 12 h. The precipitate was filtered off and washed with EtOH and Et_2O.

Method B. A solution of 7-hydroxy-3-phenoxy-8-formylchromone (**7** or **9**, 1 mmol) in DMF (2 mL) was treated with the appropriate 2-hetarylacetonitrile (1 mmol) and piperidine (three drops), heated for 5 min, held at room temperature for 12 h, treated with H_2SO_4 (10 mL, 3%), refluxed for 5 h, and cooled. The precipitate was filtered off and recrystallized from DMF.

9-(Benzthiazol-2-yl)-2-methyl-3-(4-chlorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (30). Method A (AcOH + HCl). Yield 56%, mp >300°C, $C_{26}H_{14}ClNO_5S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.74 (3H, s, CH_3-2), 6.94 (2H, d, J = 8.8, H-2′, H-6′), 7.33 (2H, d, J = 8.8, H-3′, H-5′), 7.79 (1H, d, J = 9.2, H-6), 7.96 (1H, t, J = 8.4, H-6″), 8.04 (1H, t, J = 8.4, H-5″), 8.32 (1H, d, J = 8.4, H-4″), 8.4 (1H, d, J = 8.4, H-7″), 8.88 (1H, d, J = 9.2, H-5), 9.88 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1735 ($C{=}O_\alpha$), 1640 ($C{=}O_\gamma$).

2-Methyl-9-(5-phenyl-1,3,4-thiadiazol-2-yl)-3-(4-chlorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (31). Method A (AcOH + HCl). Yield 83%, mp >300°C, $C_{27}H_{15}ClN_2O_5S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.75 (3H, s, CH_3-2), 6.94 (2H, d, J = 8.0, H-2′, H-6′), 7.32 (2H, d, J = 8.0, H-3′, H-5′), 7.78-7.81 (3H, m, H-6, H-3″, H-5″), 7.96 (1H, t, J = 7.6, H-4″), 8.18 (2H, d, J = 7.6, H-2″, H-6″), 8.82 (1H, d, J = 8.8, H-5), 9.93 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1730 ($C{=}O_\alpha$), 1650 ($C{=}O_\gamma$).

9-[4-(4-Methylphenyl)-1,3-thiazol-2-yl]-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (32). Method A (AcOH). Yield 65%, mp >300°C (DMF), $C_{28}H_{17}NO_5S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.52 (3H, s, CH_3-4‴), 7.15 (2H, d, J = 8.0, H-2′, H-6′), 7.30 (1H, t, J = 8.0, H-4′), 7.45-7.50 (4H, m, H-3‴, H-5‴, H-3′, H-5′), 7.71 (2H, d, J = 7.2, H-2‴, H-6‴), 7.78 (1H, d, J = 9.2, H-6), 8.13 (1H, s, H-5″$_{Th}$), 8.32 (1H, s, H-2), 8.91 (1H, d, J = 9.2, H-5), 9.87 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1725 ($C{=}O_\alpha$), 1650 ($C{=}O_\gamma$).

2-Methyl-9-(pyridin-2-yl)-3-(4-chlorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (33). Method A (AcOH). Yield 81%, mp 276°C (AcOH), $C_{24}H_{14}ClNO_5$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.72 (3H, s, CH_3-2), 6.94 (2H, d, J = 8.8, H-2′, H-6′), 7.33 (2H, d, J = 8.8, H-3′, H-5′), 7.78 (1H, d, J = 9.2, H-6), 8.22 (1H, m, H-4″), 8.82-8.86

(3H, m, H-3″, H-5″, H-5), 9.03 (1H, d, J = 6.0, H-6″), 9.68 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1740 ($C=O_{\alpha}$), 1645 ($C=O_{\gamma}$).

9-(6-Methyl-4-oxo-3,4-dihydroquinazolin-2-yl)-3-(4-fluorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (34). Method A (AcOH + HCl). Yield 68%, mp >300°C (DMF), $C_{27}H_{15}FN_2O_6$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.76 (3H, s, CH_3-6″), 7.15 (4H, d, J = 5.6, H-2′, H-3′, H-5′, H-6′), 7.78 (1H, d, J = 9.2, H-6), 8.08 (1H, d, J = 8.4, H-7″), 8.10 (1H, d, J = 8.4, H-8″), 8.23 (1H, s, H-2), 8.42 (1H, s, H-5″), 8.98 (1H, d, J = 9.2, H-5), 10.11 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1725 ($C=O_{\alpha}$), 1680 (C=O), 1660 ($C=O_{\gamma}$).

9-[4-(1,3-Benzodioxol-5-yl)-1,3-thiazol-2-yl]-3-phenoxy-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (35). Method A (AcOH + HCl). Yield 80%, mp >300°C, $C_{28}H_{15}NO_7S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 6.12 (2H, s, OCH_2O), 7.07 (1H, d, J = 8.4, H-7‴), 7.12 (2H, d, J = 8.0, H-2′, H-6′), 7.27 (2H, m, H-4′, H-4‴), 7.36 (1H, d, J = 8.4, H-6‴), 7.46 (2H, t, J = 8.0, H-3′, H-5′), 7.76 (1H, d, J = 9.2, H-6), 8.06 (1H, s, H-5″$_{Th}$), 8.30 (1H, s, H-2), 8.89 (1H, d, J = 9.2, H-5), 9.85 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1745 ($C=O_{\alpha}$), 1650 ($C=O_{\gamma}$).

9-(4-Methyl-1,3-thiazol-2-yl)-3-(4-fluorophenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (36). Method B. Yield 69%, mp >300°C (DMF), $C_{22}H_{12}FNO_5S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 2.84 (3H, s, CH_3-4″), 6.94 (4H, d, J = 5.6, H-2′, H-3′, H-5′, H-6′), 7.75 (1H, d, J = 9.2, H-6), 7.78 (1H, s, H-5‴$_{Th}$), 8.29 (1H, s, H-2), 8.88 (1H, d, J = 9.2, H-5), 9.69 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1735 ($C=O_{\alpha}$), 1650 ($C=O_{\gamma}$).

9-[4-(4-Bromophenyl)-1,3-thiazol-2-yl]-3-(2-methoxyphenoxy)-4*H*,8*H*-pyrano[2,3-*f*]chromen-4,8-dione (37). Yield 72%, mp 255°C (DMF), $C_{28}H_{16}BrNO_6S$. PMR spectrum (400 MHz, CF_3CO_2D, δ, ppm, J/Hz): 4.06 (3H, s, CH_3O-2′), 7.08-7.31 (4H, m, H-3′, H-4′, H-5′, H-6′), 7.69 (2H, d, J = 8.4, H-2″, H-6″), 7.75 (1H, d, J = 9.2, H-6), 7.81 (2H, d, J = 8.4, H-3″, H-5″), 8.19 (1H, s, H-5″$_{Th}$), 8.26 (1H, s, H-2), 8.91 (1H, d, J = 9.2, H-5), 9.88 (1H, s, H-10). IR spectrum (KBr, ν, cm^{-1}): 1725 ($C=O_{\alpha}$), 1660 ($C=O_{\gamma}$).

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