Multicomponent condensation of 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one with aldehydes and Meldrum´s acid

*B. V. Lichitsky, S. V. Shorunov, A. O. Osipov, A. N. Komogortsev, A. A. Dudinov, and M. M. Krayushkin**

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. E-mail: mkray@ioc.ac.ru

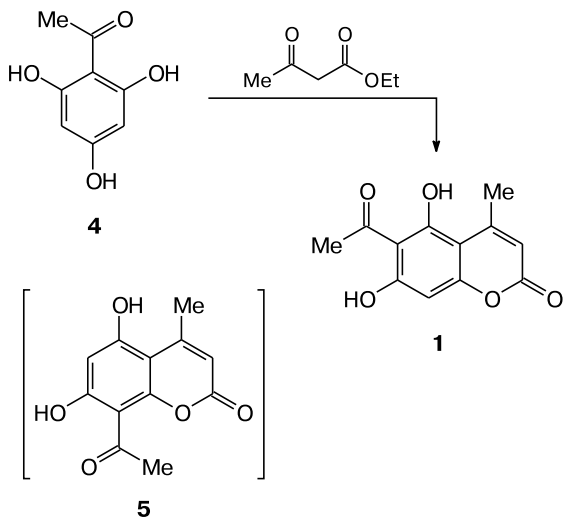
Previously unknown 6-acetyl-10-aryl-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]-chromene-2,8-diones were synthesized by multicomponent condensation of 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one, aromatic aldehydes, and Meldrum´s acid. A fundamental possibility of interconversion of substituted 6-acetyl-10-aryl-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-diones and methyl 3-(6-acetyl-5,7-dihydroxy-4-methyl-2-oxo-2*H*-chromen-8-yl)-3-arylpropionates was demonstrated.

Key words: multicomponent condensation, Meldrum´s acid, 7-hydroxycoumarins, 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one, 6-acetyl-10-aryl-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-diones, methyl 3-(6-acetyl-5,7-dihydroxy-4-methyl-2-oxo-2*H*-chromen-8-yl)-3-arylpropionates.

Derivatives of 7-hydroxycoumarin (umbelliferone) constitute an interesting family of natural compounds of plant origin. 7-Hydroxycoumarins play an important role in plant biochemistry and physiology. They act as antioxidants, enzyme inhibitors, and precursors for biosynthesis of a wide range of secondary metabolites. Cytotoxicity of natural and synthetic 7-hydroxycoumarins is well known.[1] Substituted 7-hydroxycoumarins show anticancer activity against malignant tumors, *e.g.*, prostate cancer, melanoma, and kidney tumors.[2—4] Geiparvarin, a derivative of umbelliferone, show pronounced cytostatic activity against sarcoma and lung cancer.[5,6] Natural 5,7-dihydroxycoumarin derivative, calanolide A, was suggested for an experimental anti-HIV treatment.[7] However, despite a wide variety of useful properties exhibiting by natural 7-hydroxydoumarins, most of them cannot be used as therapeutic agents due to high toxicity, cancerogenicity, and mutagenicity. Therefore, modification of natural coumarin compounds and elaboration of general synthetic procedures towards fused heterocyclic scaffolds bearing coumarin fragment is still a great challenge for organic chemists. Multicomponent reactions are regarded as an efficient instrument to achieve this goal. An advantage of this approach is the possibility to synthesize a large compound series avoiding the complex multistep reaction sequences.[8,9]

The aim of the present work is studying the multicomponent reactions between 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one (**1**), aromatic aldehydes **2**, and Meldrum´s acid **3** and examination of the structures and properties of the reaction products. The starting coumarin **1** was synthesized by the reaction of 1-(2,4,6-trihydroxyphenyl)ethanone (**4**) with ethyl acetoacetate under the Pechmann conditions (Scheme 1). It is of note that the condensation can theoretically produce isomeric 8-acetyl-5,7-dihydroxy-4-methylchromen-2-one (**5**).

Scheme 1



We attempted to establish the structure of the synthesized coumarin **1** by $^{1}H—^{13}C$ HMBC NMR technique. Unfortunately, unambiguous choice between structures **1**

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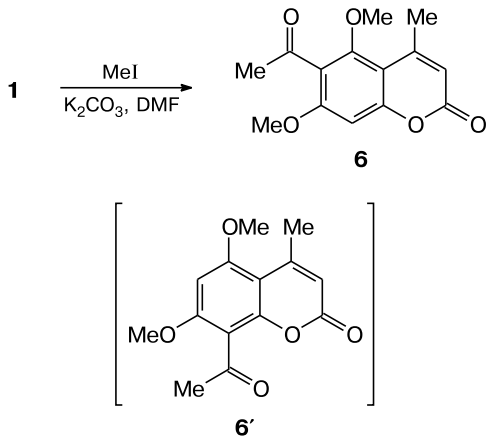
and **5** cannot be made from the $^{1}H—^{13}C$ HMBC experimental data due to the occurrence of the exchange processes involving the hydroxy groups of the synthesized compound. To solve this problem, we performed methylation of coumarin **1** to give 6-acetyl-5,7-dimethoxy-4-methylchromen-2-one (**6**) (Scheme 2).

Scheme 2



Structure of compound **6** was unambiguously established using 2D $^{1}H—^{13}C$ HMBC experiment. The carbon atoms at the positions 5 and 7 of the benzene ring (δ 155.27 and 158.50) were identified by using correlations between protons of 5-MeO and 7-MeO groups (δ 3.71 and 3.87). The proton at the 8-positon (δ 6.91) correlates with the carbon atom at the 7-positon (δ 158.50) but no correlation between the 8-positioned proton (δ 6.91) and the 5-postioned carbon atom (δ 155.27) is found. These indicate that the only one methoxy group is *ortho* to the benzene ring proton. Such spatial arrangement of the substituent corresponds only to the product **6** (in the case of structure **6′**, both methoxy groups would be *ortho* to the benzene ring proton).

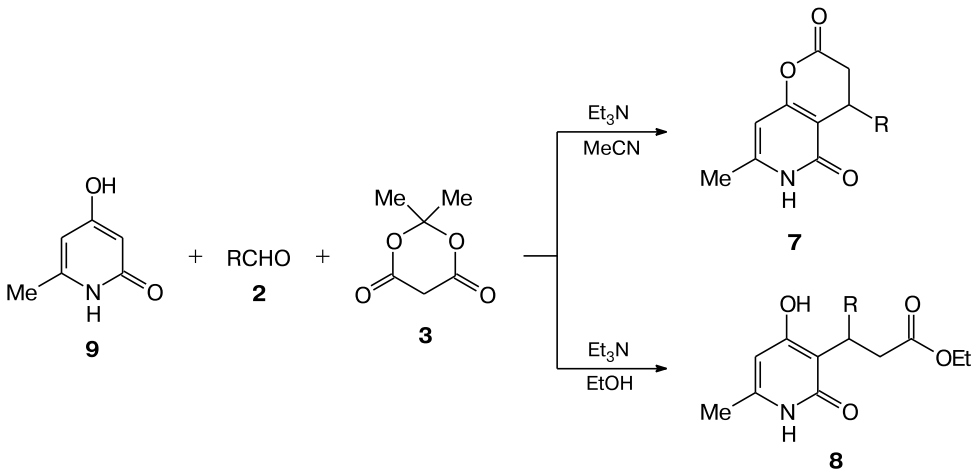
Note that we have earlier developed[10] synthetic procedures to synthesize fused dihydropyranones **7** and esters of substituted 3-arylpropionic acids **8** *via* multicomponent condensation of hydroxypyridone **9**, aldehydes **2**, and Meldrum′s acid **3**, when the reaction direction depended on the nature of the solvent used. Thus, the reaction carried out in MeCN gave dihydropyranones **7**, while in alcohols esters **8** were obtained (Scheme 3).

Based on these results (see Scheme 3), we carried out the reaction of coumarin **1** with aldehydes **2**, and Meldrum′s acid **3** in MeCN assuming to obtain derivatives of 6-acetyl-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]-chromene-2,8-dione (**10**). However, we failed to prepare lactones **10** following this procedure due apparently to their low stability under reaction conditions. To synthesize the target compounds **10**, we suggested a new one-pot procedure. The main feature of this process is performing the multicomponent reaction in methanol in the presence of triethylamine without isolation of pure intermediate methyl esters **11**. Subsequent concentrating the reaction mixture under vacuum and heating the residue in acetic acid result in dihydropyranones **10** (Scheme 4).

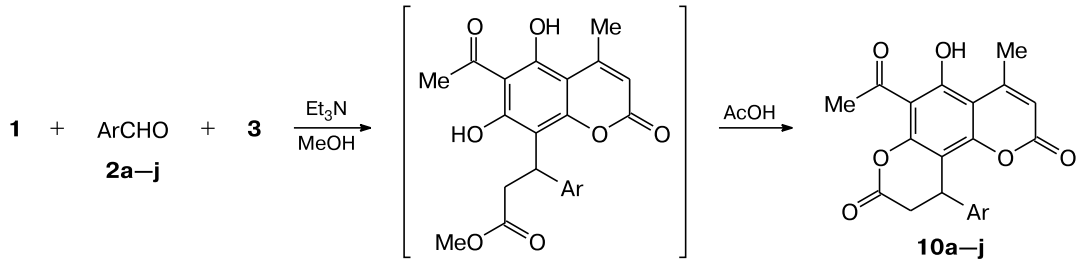
Intermediate methyl esters **11** can be isolated pure and characterized. Thus, we demonstrated the principal possibility of ring opening of the dihydropyranone cycle on treatment with nucleophiles by the synthesis of methyl 3-(6-acetyl-5,7-dihydroxy-4-methyl-2-oxo-2*H*-chromen-8-yl)-3-(4-methoxyphenyl)propionate **11b** (Scheme 5). Refluxing lactone **10b** in methanol in the presence of triethylamine gives methyl ester **11b** in good yield. Heating compound **11b** in acetic acid enables the reverse reaction resulting in the starting dihydropyranone **10b**.

In summary, we performed multicomponent condensation between 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one (**1**), aromatic aldehydes, and Meldrum′s acid. The

Scheme 3

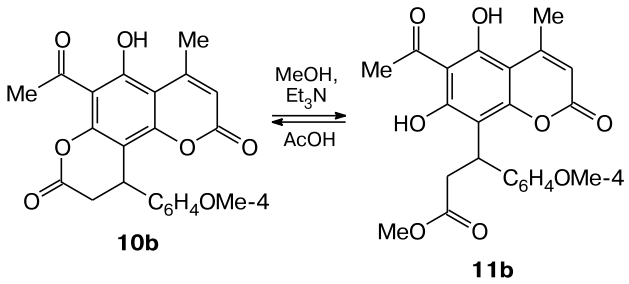


Scheme 4



10, 11	Ar	10, 11	Ar	10, 11	Ar	10, 11	Ar
a	Ph	**d**	3,4-$(MeO)_2C_6H_3$	**g**	3-HO-4-$MeOC_6H_3$	**i**	1-Naphthyl
b	4-$MeOC_6H_4$	**e**	4-$MeO_2CC_6H_4$	**h**	2,4-$Cl_2C_6H_3$	**j**	3,4-OCH_2O-C_6H_3
c	4-$MeSC_6H_4$	**f**	3,4,5-$(MeO)_3C_6H_2$				

Scheme 5



reaction direction depends on the solvent nature and reaction conditions and may produce either cyclic dihydropyranones **10** or open esters **11**. The conditions of interconversion of compounds **10** and **11** were also studied. Structures of the synthesized compounds were confirmed by ^1H and ^{13}C NMR spectroscopy and high resolution mass spectrometry.

Experimental

^1H, ^{13}C, and ^1H—^{13}C HMBC NMR spectra were run on Bruker AM-300 and Bruker AV-600 instruments (working frequencies of 300 and 600 MHz) in DMSO-d_6. High resolution electrospray ionization (ESI) mass spectrometry was performed with a Bruker micrOTOF II instrument. Melting points were measured using a Boetius apparatus and are given uncorrected.

Compound **4** was synthesized by the known procedure.[11]

6-Acetyl-5,7-dihydroxy-4-methylchromen-2-one (1). A mixture of 1-(2,4,6-trihydroxyphenyl)ethanone (**4**) (8.4 g, 50 mmol) and ethyl acetoacetate (6.83 g, 52.mmol) in 70% sulfuric acid (60 mL) was stirred at room temperature for 48 h and then treated with water (200 mL) for 5 h. The precipitate formed was collected by filtration, washed with water (3×200 mL), and recrystallized from ethanol. Yield 69%, m.p. 235—237 °C. ^1H NMR (DMSO-d_6), δ: 2.47 (s, 3 H, CH_3); 2.65 (s, 3 H, CH_3); 5.89 (s, 1 H, CH); 6.21 (s, 1 H, CH); 11.81 (br.s, 1 H, OH); 15.23 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.48, 33.00, 94.52, 102.02, 106.46, 109.84, 154.88, 159.02, 159.68, 163.68, 165.65, 205.11. MS (ESI), *m/z*: found 235.0601 $[M + H]^+$. $C_{12}H_{10}O_5$. Calculated: [M + H] = 235.0607.

6-Acetyl-5,7-dimethoxy-4-methylchromen-2-one (6). A mixture of 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one (**1**) (0.23 g, 1 mmol), anhydrous potassium carbonate (0.55 g, 4 mmol), and iodomethane (0.57 g, 4 mmol) in DMF (6 mL) was stirred at room temperature for 48 h. Then the mixture was poured into water (50 mL) and stirred for 5 h. The precipitate formed was collected by filtration and washed with water (3×20 mL). Yield 87%, m.p. 162—164 °C. ^1H NMR (DMSO-d_6), δ: 2.47 (s, 3 H, CH_3); 2.50 (s, 3 H, CH_3); 3.71 (s, 3 H, OCH_3); 3.87 (s, 3 H, OCH_3); 6.15 (s, 1 H, CH); 6.91 (s, 1 H, CH). ^{13}C NMR (DMSO-d_6), δ: 21.78, 32.26, 56.59, 64.05, 96.50, 107.48, 112.85, 122.44, 152.85, 155.27, 155.99, 158.50, 159.07, 200.27. MS (ESI), *m/z*: found 263.0914 $[M + H]^+$. $C_{14}H_{14}O_5$. Calculated: [M + H] = 263.0920.

6-Acetyl-10-aryl-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-diones 10a—j (general procedure). A mixture of 6-acetyl-5,7-dihydroxy-4-methylchromen-2-one (**1**) (0.47 g, 2 mmol), the corresponding aldehyde (2.2 mmol), Meldrum´s acid (0.36 g, 2.5 mmol), and triethylamine (0.3 g, 3 mmol) in MeOH (10 mL) was refluxed for 3 h and the volatiles were removed *in vacuo* to dryness. To the residue, acetic acid (7 mL) was added and mixture was refluxed for 4 h, cooled to room temperature, and stirred for 3 h. The precipitate formed was collected by filtration and washed with acetic acid (3×5 mL). To remove traces of AcOH, the precipitate was kept for 24 h in water (50 mL) at room temperature, collected by filtration, and washed with water (3×10 mL).

6-Acetyl-5-hydroxy-4-methyl-10-phenyl-9,10-dihydropyrano-[2,3-*f*]chromene-2,8-dione (10a). Yield 67%, m.p. 226—228 °C. ^1H NMR (DMSO-d_6), δ: 2.62 (s, 3 H, CH_3); 2.82 (s, 3 H, CH_3); 3.05 (d, 1 H, H—C—H, J = 16.0 Hz); 3.40 (m, 1 H, H—C—H); 4.83 (d, 1 H, CH, J = 5.9 Hz); 6.22 (s, 1 H, CH); 7.15—7.40 (m, 5 H, H_{Ar}); 14.89 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.62, 33.21, 33.65, 35.97, 104.64, 106.16, 106.90, 112.37, 126.58, 127.37, 129.00, 140.13, 154.55, 154.66, 155.56, 158.15, 163.13, 165.49, 204.40. MS (ESI), *m/z*: found 365.1020 $[M + H]^+$. $C_{21}H_{16}O_6$. Calculated: [M + H] = 365.1025.

6-Acetyl-5-hydroxy-10-(4-methoxyphenyl)-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10b). Yield 59%,

m.p. 265—267 °C. ^{1}H NMR (DMSO-d_6), δ: 2.59 (s, 3 H, CH_3); 2.80 (s, 3 H, CH_3); 3.01 (d, 1 H, H—C—H, J = 15.8 Hz); 3.35 (m, 1 H, H—C—H); 3.71 (s, 3 H, OCH_3); 4.75 (d, 1 H, CH, J = 5.0 Hz); 6.20 (s, 1 H, CH); 6.87 (d, 2 H, H_{Ar}, J = 7.6 Hz); 7.08 (d, 2 H, H_{Ar}, J = 7.6 Hz); 14.79 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.59, 32.89, 33.18, 36.11, 55.03, 105.08, 106.11, 106.83, 112.37, 114.34, 127.68, 131.89, 154.44, 154.61, 155.53, 158.14, 158.45, 163.03, 165.54, 204.38. MS (ESI), *m/z*: found 395.1125 $[M + H]^+$. $C_{22}H_{18}O_7$. Calculated: [M + H] = = 395.1131.

6-Acetyl-5-hydroxy-4-methyl-10-(4-methylsulfanylphenyl)-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10c). Yield 74%, m.p. 246—248 °C. ^{1}H NMR (DMSO-d_6), δ: 2.43 (s, 3 H, SCH_3); 2.60 (s, 3 H, CH_3); 2.79 (s, 3 H, CH_3); 3.02 (d, 1 H, H—C—H, J = 15.9 Hz); 3.39 (m, 1 H, H—C—H); 4.77 (d, 1 H, CH, J = 6.1 Hz); 6.22 (s, 1 H, CH); 7.10 (d, 2 H, H_{Ar}, J = 8.2 Hz); 7.21 (d, 2 H, H_{Ar}, J = 8.2 Hz); 14.81 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 14.87, 23.90, 33.44, 33.47, 36.16, 104.90, 106.43, 107.15, 112.68, 126.75, 127.47, 136.91, 137.59, 154.79, 154.90, 155.82, 158.40, 163.37, 165.73, 204.66. MS (ESI), *m/z*: found 411.0897 $[M + H]^+$. $C_{22}H_{18}O_6S$. Calculated: [M + H] = 411.0902.

6-Acetyl-5-hydroxy-10-(3,4-dimethoxyphenyl)-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10d). Yield 58%, m.p. 195—197 °C. ^{1}H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, CH_3); 2.80 (s, 3 H, CH_3); 3.08 (d, 1 H, H—C—H, J = 15.8 Hz); 3.35 (m, 1 H, H—C—H); 3.69 (s, 3 H, OCH_3); 3.75 (s, 3 H, OCH_3); 4.75 (d, 1 H, CH, J = 5.6 Hz); 6.22 (s, 1 H, CH); 6.45 (d, 1 H, H_{Ar}, J = 7.8 Hz); 6.82 (d, 1 H, H_{Ar}, J = 7.8 Hz); 6.95 (s, 1 H, H_{Ar}); 14.82 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.60, 33.17, 33.20, 36.02, 55.44, 55.48, 104.91, 106.09, 106.81, 110.99, 111.88, 112.33, 117.79, 132.36, 148.10, 149.05, 154.45, 154.63, 155.56, 158.17, 163.02, 165.61, 204.37. MS (ESI), *m/z*: found 425.1231 $[M + H]^+$. $C_{23}H_{20}O_8$. Calculated: [M + H] = = 425.1236.

Methyl 4-(6-acetyl-5-hydroxy-4-methyl-2,8-dioxo-9,10-dihydro-2*H*,8*H*-pyrano[2,3-*f*]chromen-10-yl)benzoate (10e). Yield 83%, m.p. 263—265 °C. ^{1}H NMR (DMSO-d_6), δ: 2.59 (s, 3 H, CH_3); 2.80 (s, 3 H, CH_3); 3.07 (d, 1 H, H—C—H, J = 16.0 Hz); 3.47 (dd, 1 H, H—C—H, J = 16.0 Hz, J = 5.8 Hz); 3.82 (s, 3 H, OCH_3); 4.90 (d, 1 H, CH, J = 5.8 Hz); 6.20 (s, 1 H, CH); 7.33 (d, 2 H, H_{Ar}, J = 7.7 Hz); 7.90 (d, 2 H, H_{Ar}, J = 7.7 Hz); 14.82 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.60, 33.18, 33.69, 35.62, 52.11, 103.96, 106.21, 106.93, 112.44, 127.15, 128.83, 129.85, 145.53, 154.60, 155.59, 158.05, 163.24, 165.21, 165.80, 168.84, 204.39. MS (ESI), *m/z*: found 423.1074 $[M + H]^+$. $C_{23}H_{18}O_8$. Calculated: [M + H] = = 423.1080.

6-Acetyl-5-hydroxy-4-methyl-10-(3,4,5-trimethoxyphenyl)-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10f). Yield 62%, m.p. 229—231 °C. ^{1}H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, CH_3); 2.80 (s, 3 H, CH_3); 3.08 (d, 1 H, H—C—H, J = 16.0 Hz); 3.36 (m, 1 H, H—C—H); 3.61 (s, 3 H, OCH_3); 3.69 (s, 6 H, OCH_3); 4.75 (d, 1 H, CH, J = 6.3 Hz); 6.23 (s, 1 H, CH); 6.44 (s, 2 H, H_{Ar}); 14.80 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.61, 33.23, 33.81, 35.87, 55.91, 59.89, 104.05, 104.55, 106.16, 106.84, 112.39, 135.83, 136.79, 153.10, 154.45, 154.62, 155.61, 158.19, 163.07, 165.69, 204.43. MS (ESI), *m/z*: found 455.1337 $[M + H]^+$. $C_{24}H_{22}O_9$. Calculated: [M + H] = 455.1342.

6-Acetyl-5-hydroxy-10-(3-hydroxy-4-methoxyphenyl)-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10g). Yield 72%, m.p. 293—295 °C. ^{1}H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, CH_3); 2.80 (s, 3 H, CH_3); 2.97 (d, 1 H, H—C—H, J = 15.9 Hz); 3.34 (m, 1 H, H—C—H); 3.71 (s, 3 H, OCH_3); 4.66 (d, 1 H, CH, J = 5.8 Hz); 6.22 (s, 1 H, CH); 6.52 (d, 1 H, H_{Ar}, J = 8.0); 6.57 (s, 1 H, H_{Ar}); 6.83 (d, 1 H, H_{Ar}, J = 8.0 Hz); 9.00 (s, 1 H, OH); 14.78 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.60, 32.99, 33.18, 36.06, 55.59, 105.25, 106.07, 106.79, 112.38, 112.60, 113.86, 117.04, 132.54, 146.72, 146.90, 154.38, 154.61, 155.54, 158.16, 162.93, 165.56, 204.34. MS (ESI), *m/z*: found 411.1074 $[M + H]^+$. $C_{22}H_{18}O_8$. Calculated: [M + H] = = 411.1080.

6-Acetyl-10-(2,4-dichlorophenyl)-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10h). Yield 68%, m.p. 232—234 °C. ^{1}H NMR (DMSO-d_6), δ: 2.59 (s, 3 H, CH_3); 2.82 (s, 3 H, CH_3); 2.90 (d, 1 H, H—C—H, J = 16.1 Hz); 3.51 (dd, 1 H, H—C—H, J = 16.1 Hz, J = 6.2 Hz); 5.09 (d, 1 H, CH, J = 6.2 Hz); 6.20 (s, 1 H, CH); 6.89 (d, 1 H, H_{Ar}, J = 7.8 Hz); 7.30 (d, 1 H, H_{Ar}, J = 7.8 Hz); 7.75 (s, 1 H, H_{Ar}); 14.86 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.54, 31.26, 33.16, 33.99, 102.97, 106.28, 106.83, 112.48, 128.05, 128.99, 129.72, 133.20, 133.33, 136.09, 154.43, 155.05, 155.42, 157.84, 163.51, 164.65, 204.39. MS (ESI), *m/z*: found 433.0240 $[M + H]^+$. $C_{21}H_{14}Cl_2O_6$. Calculated: [M + H] = 433.0246.

6-Acetyl-5-hydroxy-4-methyl-10-(1-naphthyl)-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10i). Yield 74%, m.p. 273—275 °C. ^{1}H NMR (DMSO-d_6), δ: 2.61 (s, 3 H, CH_3); 2.85 (s, 3 H, CH_3); 2.98 (d, 1 H, H—C—H, J = 15.7 Hz); 3.57 (dd, 1 H, H—C—H, J = 15.7 Hz, J = 6.6 Hz); 5.68 (d, 1 H, CH, J = 6.6 Hz); 6.18 (s, 1 H, CH); 6.88 (m, 1 H, H_{Ar}); 7.33 (m, 1 H, H_{Ar}); 7.64 (m, 1 H, H_{Ar}); 7.72 (m, 1 H, H_{Ar}); 7.87 (m, 1 H, H_{Ar}); 8.03 (m, 1 H, H_{Ar}); 8.40 (m, 1 H, H_{Ar}); 14.92 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.62, 30.41, 33.21, 35.66, 104.47, 106.29, 106.86, 112.35, 123.08, 123.20, 125.48, 126.18, 126.94, 128.20, 129.08, 129.92, 133.88, 135.35, 154.66, 155.33, 155.49, 158.03, 163.33, 165.21, 204.52. MS (ESI), *m/z*: found 415.1176 $[M + H]^+$. $C_{25}H_{18}O_6$. Calculated: [M + H] = 415.1182.

6-Acetyl-10-(benzo[1,3]dioxol-5-yl)-5-hydroxy-4-methyl-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10j). Yield 65%, m.p. 268—270 °C. ^{1}H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, CH_3); 2.79 (s, 3 H, CH_3); 3.01 (d, 1 H, H—C—H, J = 15.8 Hz); 3.35 (m, 1 H, H—C—H); 4.72 (d, 1 H, CH, J = 6.0 Hz); 5.99 (s, 2 H, OCH_2O); 6.21 (s, 1 H, H_{Ar}); 6.53 (d, 1 H, H_{Ar}, J = 7.8 Hz); 6.82 (m, 2 H, H_{Ar}); 14.84 (br.s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 23.94, 33.52, 33.66, 36.51, 101.44, 105.08, 106.46, 107.15, 107.60, 108.75, 112.70, 119.76, 134.16, 146.82, 148.09, 154.84, 154.95, 155.86, 158.48, 163.47, 165.80, 204.70. MS (ESI), *m/z*: found 409.0918 $[M + H]^+$. $C_{22}H_{16}O_8$. Calculated: [M + H] = = 409.0923.

Methyl 3-(6-acetyl-5,7-dihydroxy-4-methyl-2-oxo-2*H*-chromen-8-yl)-3-(4-methoxyphenyl)propionate (11b). A mixture of compound **10b** (0.39 g, 1 mmol) and triethylamine (0.2 g, 2 mmol) in MeOH (5 mL) was refluxed for 3 h. The reaction mixture was cooled, treated with concentrated HCl (0.3 g) and water (5 mL), and stirred for 3 h at room temperature. The precipitate formed was collected by filtration and washed with 50% aqueous MeOH (3×7 mL). Yield 61%, m.p. 254—256 °C. ^{1}H NMR (DMSO-d_6), δ: 2.53 (s, 3 H, CH_3); 2.68 (s, 3 H, CH_3); 3.22 (dd, 1 H, H—C—H, J = 16.0 Hz, J = 7.8 Hz); 3.42 (dd, 1 H, H—C—H, J = 16.0 Hz, J = 7.8 Hz); 3.51 (s, 3 H, OCH_3); 3.68 (s, 3 H, OCH_3); 5.11 (t, 1 H, CH, J = 7.8 Hz); 6.00 (s, 1 H, CH); 6.81 (d, 2 H, H_{Ar}, J = 8.4 Hz); 7.23 (d, 2 H, H_{Ar}, J = 8.4 Hz). ^{13}C NMR (DMSO-d_6), δ: 23.88, 32.12, 34.35, 36.44, 51.31, 54.93, 103.92, 110.18, 110.98, 113.24, 113.44,

128.18, 133.99, 155.28, 157.48, 158.51, 158.54, 160.56, 161.16, 172.26, 205.49. MS (ESI), *m/z*: found 449.1207 $[M + Na]^+$. $C_{23}H_{22}O_8$. Calculated: [M + Na] = 449.1212.

Synthesis of 6-acetyl-5-hydroxy-4-methyl-10-(4-methoxyphenyl)-9,10-dihydropyrano[2,3-*f*]chromene-2,8-dione (10b) from methyl ester 11b. A solution of methyl ester **11b** (0.43 g, 1 mmol) in acetic acid (5 mL) was refluxed for 4 h, cooled, and stirred at room temperature for 3 h. The precipitate formed was collected by filtration and washed with acetic acid (3×5 mL). To remove traces of acetic acid, the precipitate was kept in water (50 mL) for 24 h, filtered, and washed with water (3×10 mL). Yield 65%. Melting point and ^{1}H NMR spectrum of compound **10b** are identical to those of the sample obtained by multicomponent condensation **1** + **2b** + **3**.

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