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Graphical Abstract

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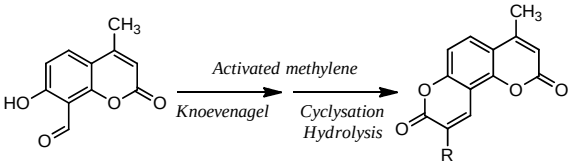

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Synthesis of novel 2*H*,8*H*-pyrano[2,3-*f*]chromene-2,8-diones from 8-formyl-7-hydroxy-4-methylcoumarin

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ABSTRACT

We report the synthesis of novel 2*H*,8*H*-pyrano[2,3-*f*]chromene-2,8-dione based scaffolds by the reaction of 8-formyl-7-hydroxy-4-methylcoumarin with various active methylene compounds. A mechanism of a tandem Knoevenagel condensation and cyclisation reaction is proposed. The structure of all compounds was established on the basis of ^{1}H and ^{13}C NMR data, high resolution mass spectrometry and elemental analysis.

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1. **Introduction**[*]

Coumarins and pyran-2-ones form an exceptional class of oxygen containing heterocyclic compounds playing a key role in the medicinal area due to their structural diversity and pharmaceutical properties. They are exemplified in a large number of natural products displaying a broad spectrum of medicinal benefits. Various synthetic coumarin derivatives constitute one of the most widely used groups of anti-HIV,[1] anti-inflammatory[2-4] and antioxidant[5,6] agents. They have been extensively investigated for decades to exert other valuable biological effects such as the anticancer[7-10] and the antiviral activities.[11] In light of these potential biological findings, a huge amount of researches on coumarin derivatives have been conducted to develop a plethora of synthetic procedures mostly by using Perkin or Knoevenagel reactions.[12-18] However, further scientific efforts are still on demand to seek for more adequate and flexible synthetic methodologies of novel coumarin based scaffolds. Taking into consideration the referred biological outcome due to pyran-2-ones, our interest is particularly focused on the chemical transformations related to triacetic lactone (4-hydroxy-6-methylpyran-2-one, TAL) **3a** (Scheme 2).[19-21] Herein, we report an efficient synthetic procedure of 8-formyl-7-hydroxy-4-methylcoumarin **2** in view of investigating its reactivity towards the above mentioned pyran-2-one **3a** and other active methylene compounds such as, ethyl acetoacetate **3b**, malononitrile **3c** and ethyl cyanoacetate **3d**. The use of the key starting material **2** in the current study provides a facile access to a novel series of 2*H*,8*H*-pyrano[2,3-*f*]chromene-2,8-dione based scaffolds **4a-d** via a Knoevenagel condensation / cyclisation tandem process. Synthetic pyranobenzopyranone derivatives have recently been described as photoreagents towards DNA and present some antimicrobial activity in the dark.[22]

2. Results and discussion

A large number of investigations have been carried out on the formylation of 7-hydroxy-4-methylcoumarin **1** which usually proceeds in the presence of hexamine in refluxing acetic acid lasting for more than 6 hours of reaction time. Nevertheless, the reported strategies have not escaped criticism since this reaction is mostly offering 8-formyl-7-hydroxy-4-methylcoumarin **2** in very low yields,[23-27] and many difficulties are faced in the purification of this product **2**. However, successful attempts have been described by Panel *et al*[28] and Wei *et al*[29] affording up to 60% yield of **2**. The synthesis of **2** was repeated by us following exactly the reported operating conditions,[28,29] but only 25 % yield is reached after 8 hours of reaction time.[30] Moreover, the final product requires further steps of purification. These operative problems drive us to study the formylation reaction of 7-

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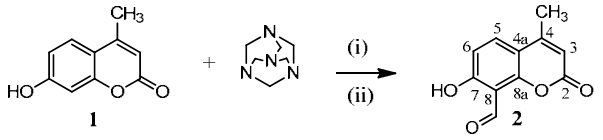
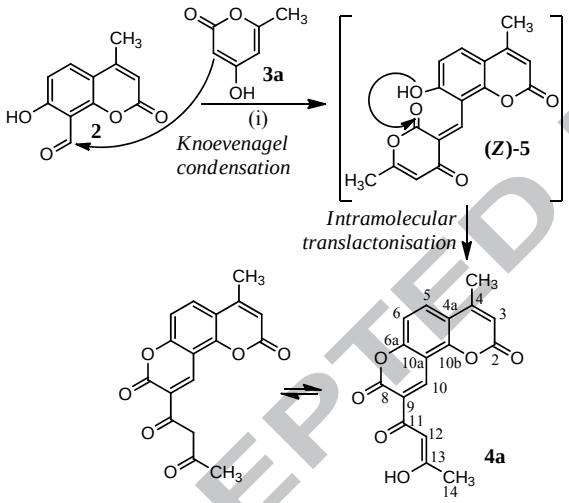
hydroxy-4-methylcoumarin **1** under the same conditions but using microwave irradiation as an alternative source of heating. By applying a power of 300 W for 7 min and 200 W after addition of HCl (20%) for 4 min, compound **2** was obtained in 40% yield.[31] The structure of **2** was confirmed on the basis of physicochemical and literature data (Scheme 1).[28,29]



Scheme 1. Synthesis of compound **2**: (i) AcOH, MW, reflux, (ii) HCl (20%), MW, 80 °C.

In our previous work, we reported that the condensation of triacetic lactone (TAL) **3a** with salicylaldehydes produces 3-acetoacetylcoumarin compounds following a successive Knoevenagel condensation and an intramolecular translactonisation.[19-22] In this undertaken study, a similar approach was used to selectively synthesize 4-methyl-9-(3-oxobutanoyl)-2*H*,8*H*-pyrano[2,3-*f*]chromene-2,8-dione **4a** through the reaction of TAL **3a** with 8-formyl-7-hydroxy-4-methylcoumarin **2**. The reaction proceeds at room temperature in a mixture of ethanol:toluene as solvent using a catalytic amount of triethylamine as base (Scheme 2).



Scheme 2. Synthesis of compounds **4a**: (i) NEt_3, toluene/EtOH, r.t.

The analytical data of the obtained product **4a**[32] indicates that a stoichiometric condensation reaction of TAL **3a** with 8-formyl-7-hydroxy-4-methylcoumarin **2** has taken place followed by water elimination as revealed by the mass spectrum resulting the molecular ion $[M+Na]^+$ at m/z 335. This fact was further supported by elemental analysis of **4a** to identify its exact molecular formula $C_{17}H_{12}O_6$. The ^1H NMR spectrum of compound **4a** presents two signals as singlets at 2.29 and 2.50 ppm assigned to the protons of the two methyl groups. Two doublet signals are observed at 7.29 and 7.83 ppm which are attributed to adjacent aromatic protons H-6 and H-5, respectively. Further characteristic singlets appearing at 6.36, 6.98 and 9.20 ppm are due to proton resonances of H-3 and H-10 related to both pyran-2-one rings and the enolic proton H-12, respectively. Finally, the appearance of a hydroxyl proton at 15.73 ppm suggests the predominance of the enolic form in the acetoacetyl moiety (in $CDCl_3$ solution) and this high frequency value thereof explains the strong intramolecular hydrogen bond with the oxygen of the C-11 carbonyl group. The ^{13}C NMR spectrum presents two signals at 170.6 and 200.2 ppm which are respectively attributed to the carbonyl groups C-11 and C-13 of the acetoacetyl enolic form. It is also possible to observe both signals of the carbonyl groups C-8 and C-2 of the pyran-2-one rings appearing at 158.9 and 156.9 ppm. A careful analysis of the HSQC spectrum helped us to assign all the protonated carbons, while the connectivities encountered in the HMBC spectrum confirm without ambiguity the structure of compound **4a** allowing the assignment of all carbonyl groups and quaternary carbons (Figure 1).

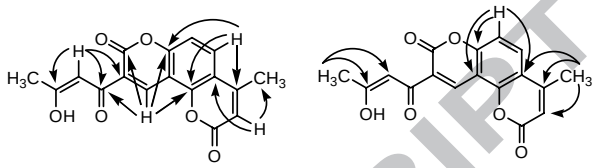


Figure 1. HMBC connectivities of compound **4a**.

The structure of **4a** is undoubtedly showing that the reaction of **2** with TAL **3a** involves a first Knoevenagel condensation affording the intermediate **5** which is ready for a subsequent intramolecular translactonisation causing the pyran-2-one ring opening of the attached TAL unit (Scheme 2).

Following our interest on the behaviour of pyran-2-one as a cyclic active methylene, we attempt the reaction of 8-formyl-7-hydroxy-4-methylcoumarin **2** with an equivalent amount of ethyl acetoacetate **3b** at room temperature in the presence of catalytic amount of piperidine (Scheme 3). The reaction was monitored by TLC which shows the formation of a unique product **4b** in very good yield (80%) after 2 hours of reaction time. The structure of this product was confirmed by mass spectrometry, elemental analysis and precisely elucidated by NMR as 9-acetyl-4-methyl-2*H*,8*H*-pyrano[2,3-*f*]chromene-2,8-dione **4b**.[33] In this case, the Knoevenagel condensation of 8-formyl-7-hydroxy-4-methylcoumarin **2** on ethyl acetoacetate **3b** can give rise to both isomeric (*E* and *Z*)-forms of the intermediate olefin **6**. However, the occurring intramolecular transesterification reaction which led to the final product **4b** occurred via the (*Z*)-configured intermediate (*Z*)-**6** (Scheme 3).

In contrast, the reaction of **2** with malononitrile **3c** has led, after a Knoevenagel reaction, to a spontaneous heterocyclisation of the 7-hydroxy group on the cyano function in the intermediate **7** delivering 8-imino-4-methyl-2-oxo-2*H*,8*H*-pyrano[2,3-*f*]chromene-9-carbonitrile **4c** in 80% yield.[34] The hydrolysis of **4c** with hydrochloric acid (4 N) under microwave irradiation (at 300 W for 4 min) affords the mono-hydrolysed product **9**.[35] Using a longer reaction time (9 min) in a more concentrated hydrochloric acid (12 N), the 9-cyano group was also hydrolysed to a carboxylic acid function in the product **10**[36] (85%, Scheme 3).

In order to study and compare the orientation of the transesterification *versus* the iminocoumarin heterocyclisation arising from both of the ethyl acetoacetate **3b** and malononitrile **3c** action on **2**, respectively, we treated 8-formyl-7-hydroxy-4-methylcoumarin **2** with ethyl cyanoacetate **3d** under similar conditions to those described above. The active methylene **3d** is also expected to provide the Knoevenagel adduct as an intermediate of two possible isomeric configuration (*E*)-**8** and (*Z*)-**8**. According to NMR and other analytical data, the iminocoumarin **4d**[37] was the major isolated compound, which was formed through the (*E*)-configured Knoevenagel adduct (*E*)-**8**. This result is completely different from those obtained by Moskvina and Khilya[38] in the reaction of 8-formyl-7-hydroxy-4-phenylcoumarin (similar to our starting material **2**) with ethyl cyanoacetate **3d**. We have used organocatalytic conditions while they used an inorganic base ($NaHCO_3$) in the condensation of 8-formyl-7-hydroxy-4-phenylcoumarin with **3d**, followed by acidic transesterification to

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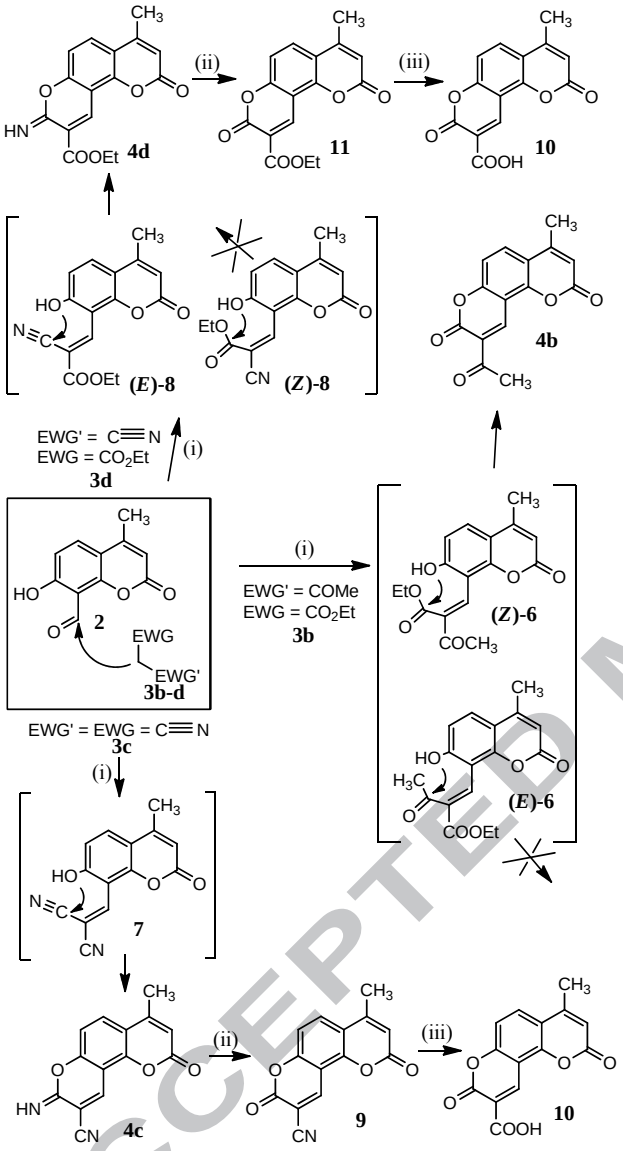
selectively produce 2*H*,8*H*-pyrano[2,3-f]chromen-4-phenyl-9-carbonitriles after acidic hydrolysis.

The hydrolysis of **4d** in hydrochloric acid 4 N under microwave irradiation (at 100 W for 4 min) yields the product **11**.[39] When the reaction time was extended to 15 min in the presence hydrochloric acid 12 N, the product **10**[36] was again obtained in a different manner (Scheme 3).



Scheme 3. Synthesis of 4-methyl-2,8-dioxo-2*H*,8*H*-pyrano[2,3-*f*]chromenes: (i) piperidine, EtOH, r.t.; (ii) HCl 4 N, MW; (iii) HCl 12 N, MW.

3. Conclusion

This paper has given an account on different chemical transformations of 8-formyl-7-hydroxy-4-methylcoumarin upon treatment with the cyclic triacetic lactone or several acyclic active methylene compounds. These organic reactions have led to the production of a novel series of functionalized 2*H*,8*H*-pyrano[2,3-*f*]chromene-2,8-dione scaffolds through a tandem process of a Knoevenagel condensation and stereoselective intramolecular translactonisation, transesterification or heterocyclisation. In this synthetic work, we have also presented an experimental improvement in the formylation reaction of 7-hydroxy-4-methylcoumarin by using microwave irradiation in a short reaction time.

Acknowledgments

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30. *8-Formyl-7-hydroxy-4-methylcoumarin **2***: Under classical heating conditions, a solution of 7-hydroxy-4-methylcoumarin **1** (5 g, 0.03 mol) and hexamethylenetetramine (10 g, 0.09 mol) in glacial acetic acid (40 mL) was refluxed for 8 h. The hexamine adduct so formed was hydrolysed with 20% HCl (75 mL) and the solution was heated for another 30 min at 70-80 °C. After cooling, the reaction solution was extracted with diethyl ether. The ether layer was evaporated and the pale yellow coloured solution was poured to crushed ice to get

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the pale yellow solid of 8-formyl-7-hydroxy-4-methylcoumarin **2** which was recrystallized from a mixture of ethanol and 1,4-dioxane. This compound was obtained as pale yellow small crystal **2**. Yield: 25%; mp.174-176 °C (mp 174-176 °C).[28,29]

31. *8-Formyl-7-hydroxy-4-methylcoumarin 2*: Under microwave irradiation, a solution of 7-hydroxy-4-methylcoumarin **1** (5 g, 0.03 mol) and hexamethylenetetramine (10 g, 0.09 mol) in glacial acetic acid (40 mL) was heated on MW irradiation at 300 W for 7 min. The hexamine adduct so formed was hydrolysed with 20% HCl (75 mL) and the solution was heated for another 4 min on MW irradiation at 200 W. After cooling, the reaction solution was extracted with diethyl ether. The ether layer was evaporated and the pale yellow coloured solution was poured to crushed ice to get the pale yellow solid of 8-formyl-7-hydroxy-4-methylcoumarin **2** which was recrystallized from a mixture of ethanol and 1,4-dioxane. This compound was obtained as pale yellow small crystal **2**. Yield: 40%; mp.174-176 °C (mp 174-176 C°).[28,29]

32. *4-Methyl-9-(3-oxobutanoyl)-2H,8H-pyrano[2,3-f]chromene-2,8-dione* **4a**. A solution of 8-formyl-7-hydroxy-4-methylcoumarin-2-one **2** (2.04 g, 0.01 mol) in toluene (10 mL) and 4-hydroxy-6-methyl-2*H*-pyran-2-one **3a** (1.26 g, 0.01 mol) in ethanol (10 mL) with some drops of NEt_3 as a catalyst was stirred at room temperature for 2 h. After reaction completion the precipitate was filtrated and recrystallized from DMF. This compound was obtained as yellow powder **4a**. Yield: 70%; mp. 252 °C; UV (λ): 360 cm^{-1}; IR (□, cm^{-1}): 3433, 3057, 2923, 1739, 1618, 1091; ^{1}H NMR ($CDCl_3$): δ 2.29 (s, 3H, H-14), 2.50 (s, 3H, 4-C*H*$_3$), 6.36 (s, 1H, H-3), 6.98 (s, H, H-12, enol), 7.30 (d, 1H, *J* = 9.0 Hz, H-6), 7.84 (d, 1H, *J* = 9.0 Hz, H-5), 9.20 (s, H, H-10), 15.70 (s, 1H, 13-O*H*); ^{13}C NMR ($CDCl_3$): δ 18.9 (4-*C*H$_3$), 27.7 (C-14), 101.8 (C-12), 108.4 (C-10a), 112.5 (C-6), 114.4 (C-3), 115.9 (C-4a), 120.9 (C-9), 129.1 (C-5), 138.8 (C-10), 150.8 (C-10b), 152.0 (C-4), 155.8 (C-6a), 156.9 (C-8), 158.9 (C-2), 170.6 (C-11), 200.2 (C-13). HRMS (ESI^+): m/z calcd for $[C_{17}H_{12}O_6+Na]^+$ 335.0532, found: 335.0535. Anal. Calcd. for $C_{17}H_{12}O_6$: C 65.39, H 3.87. Found: C 65.43, H 4.02%.

33. *9-Acetyl-4-methyl-2H,8H-pyrano[2,3-f]chromene-2,8-dione* **4b**. A solution of 8-formyl-7-hydroxy-4-methylcoumarin-2-one **2** (2.04 g, 0.01 mol) and ethyl acetoacetate **3b** (1.3 g, 0.01 mol) in ethanol (10 mL) with piperidine (0.25 mL) as a catalyst was stirred for about 2 h at room temperature. After reaction completion the obtained solid was filtrated and then crystallized from ethanol to afford pure product, as a white solid **4b**. Yield: 80%; mp. 249 °C; UV (λ): 308 cm^{-1}; IR (□, cm^{-1}): 3086, 1748, 1721, 1681, 1628, 1390, 1293, 1107, 1023; ^{1}H NMR (DMSO-d_6): δ 2.48 (s, 3H, C*H*$_3$), 2.50 (s, 3H, 4-C*H*$_3$), 6.47 (s, 1H, H-3), 7.46 (d, 1H *J* = 9.0 Hz, H-6), 8.10 (d, 1H, *J* = 9.0 Hz, H-5), 8.69 (s, 1H, H-10), ^{13}C NMR **(**DMSO-d_6): δ 18.9 (4-*C*H$_3$), 30.6 (*C*H$_3$), 107.8 (C-10a), 113.9 (C-6), 114.4 (C-3), 116.2 (C-4a), 124.8 (C-9), 131.5 (C-5), 139.8 (C-10), 151.2 (C-10b), 154.0 (C-4), 156.7 (C-6a), 158.2 (C-8), 159.1 (C-2), 195.0 (9-*C*OCH$_3$). HRMS (ESI^+): m/z calcd for $[C_{15}H_{10}O_5+Na]^+$ 293.0426, found: 293.0449. Anal. Calcd. for $C_{15}H_{10}O_5$: C 66.67, H 3.73. Found: C 66.80, H 3.83%.

34. *8-Imino-4-methyl-2-oxo-2H,8H-pyrano[2,3-f]chromene-9-carbonitrile* **4c**: A solution of 8-formyl-7-hydroxy-4-methylcoumarin-2-one **2** (2.04 g, 0.01 mol) and malononitrile **3c** (0.66 g, 0.01 mol) in ethanol (10 mL) with piperidine (0.25 mL) as a catalyst was stirred for about 2 h at room temperature. After reaction completion the obtained precipitate was filtrated and crystallized from ethanol to afford a pure pink product **4c**. Yield: 80%; mp. 229 °C; UV, λ. 310 cm^{-1}, IR (□, cm^{-1}): 3357, 2943, 2191, 1739, 1618, 1381, 1274; ^{1}H NMR (DMSO-d_6): δ 2.58 (s, 3H, 4-C*H*$_3$), 6.32 (s, 1H, H-3), 6.95 (d, 1H, *J* = 9.0 Hz, H-6), 7.77 (d, 1H, *J* = 9.0 Hz, H-5), 8.10 (s, 1H, N*H*), 8.37 (s, 1H, H-10); ^{13}C NMR (DMSO-d_6): δ 18.9 (4-*C*H$_3$), 103.0 (*C*N), 107.1 (C-10a), 113.1 (C-6), 114.4 (C-3 and C-4a), 116.0 (C-9), 132.0 (C-5), 146.0 (C-10), 150.0 (C-10b), 153.0 (C-4), 156.3 (C-6a), 158.0 (C-8 and C-2). HRMS (ESI^+): m/z calcd for $[C_{14}H_8N_2O_3+Na]^+$ 275.0433, found: 275.0399. Anal. Calcd. for $C_{14}H_8N_2O_3$: C 66.67, H 3.20, N 11.11. Found: C 66.44, H 3.07, N 11.20%.

35. *4-Methyl-2,8-dioxo-2H,8H-pyrano[2,3-f]chromene-9-carbonitrile* **9:** The solution of 8-imino-4-methyl-2-oxo-2*H*,8*H*-pyrano[2,3-*f*]chromene-9-carbonitrile **4c** (2.52 g, 0.01 mol) with acid HCl 4 N (10 mL) was stirred under MW irradiation at 300 W for 9 min. After reaction completion the precipitate was filtrated and washed with water to afford a pure yellow product **9** (85%); mp. 272 °C; UV (λ): 310 cm^{-1}; IR (□, cm^{-1}): 3380, 2915, 2236, 1739, 1627, 1579, 1381, 1274, ^{1}H NMR **(**DMSO-d_6): δ 2.50 (s, 3H, 4-C*H*$_3$), 6.51 (s, 1H, H-3), 8.166 (d, 1H, *J* = 9.0 Hz, H-5), 7.44 (d, 1H, *J* = 9.0 Hz, H-6), 9.15 (s, 1H, H-10); ^{13}C NMR (DMSO-d_6): δ 18.3 (4-*C*H$_3$), 102.7 (*C*N), 107.0 (C-10a), 112.7 (C-6), 113.7 (C-3), 114.1 (C-4a), 116.1 (C-9), 131.8 (C-10), 146.5 (C-5), 149.9 (C-10b), 153.3 (C-4), 155.5 (C-6a), 156.2 (C-8), 158.3 (C-2). MS (ESI^+): m/z found for $[C_{14}H_7NO_4]^+$ 253.00. Anal. Calcd. for $C_{14}H_7NO_4$: C 66.41, H 2.79, N 5.53. Found: C 66.50, H 2.81, N 5.66%.

36. *4-Methyl-2,8-dioxo-2H,8H-pyrano[2,3-f]chromene-9-carboxylic acid* **10**: The solution of 4-methyl-2,8-dioxo-2*H*,8*H*-pyrano[2,3-*f*]chromene-9-carbonitrile **9** (2.53 g, 0.01 mol) with acid HCl 12 N (10 mL) was stirred about 15 min under MW irradiation at 300 W. After reaction completion the precipitate was filtrated and washed with water to afford a pure white product **10** (80%), mp. 287 °C; UV (λ): 310 cm^{-1}; IR (□, cm^{-1}): 3150, 3086, 1785, 1715, 1621, 1376, 1291, 1117; ^{1}H NMR (DMSO-d_6): δ 2.48 (s, 3H, 4-C*H*$_3$), 6.49 (s, 1H, H-3), 8.12 (d, 1H, *J* = 9.0 Hz, H-5), 7.44 (d, 1H, *J* = 9.0 Hz, H-6), 8.78 (s, 1H, H-10); ^{13}C NMR (DMSO-d_6): δ 18.9 (4-*C*H$_3$), 107.6 (C-10a), 112.8 (C-6), 113.8 (C-3), 116.1 (C-4a), 118.9 (C-9), 131.3 (C-5), 141.0 (C-10), 150.9 (C-10b), 154.0 (C-4), 156.0 (C-6a), 156.8 (C-8), 159.2 (C-2), 164.0 (9-*C*OOH). MS (ESI^+): m/z found for $[C_{14}H_8O_6]^{+\bullet}$ 272. Anal. Calcd. for $C_{14}H_8O_6$: C 61.77, H 2.96. Found: C 61.90, H 3.12%.

37. *8-Imino-4-methyl-2-oxo-2H,8H-pyrano[2,3-f]chromene-9-carboxylate* **4d**. A solution of 8-formyl-7-hydroxy-4-methylcoumarin-2-one **2** (2.04 g, 0.01 mol) and ethyl cyanoacetate **3d** (1.131 g, 0.01 mol) in ethanol (10 mL) with piperidine (0.25 mL) as a catalyst was stirred for about 2 h at room temperature. After reaction completion the precipitate was filtrated and recrystallized from ethanol to afford a pure pink product **4d**. Yield: 80%; mp. 190 °C; UV (λ): 310 cm^{-1}; IR (□, cm^{-1}): 3321, 1740, 1628, 1391, 1274, 1121, 1021; ^{1}H NMR (DMSO-d_6): δ 1.38 (t, 3H, *J* = 7.2 Hz, 3H, CH_2CH_3), 2.50 (s, 3H, 4-C*H*$_3$), 4.41 (q, 2H, *J* =7.2 Hz, C*H*$_2$CH$_3$), 6.40 (s, 1H, 3-H), 7.36 (d, 1H, *J* = 9.0 Hz, H-6), 7.90 (d, 1H, *J* = 9.0 Hz, H-5), 8.90 (s, 1H, H-10), 9.60 (s, 1H, N*H*); ^{13}C NMR (DMSO-d_6): 14.2 (CH_2CH_3), 18.9 (4-*C*H$_3$), 62.2 (*C*H$_2$CH$_3$), 107.2 (C-10a), 112.5 (C-6), 113.4 (C-3), 115.2 (C-4a and C-9), 129.4 (C-5), 134.6 (C-10), 150.6 (C-10b), 152.5 (C-4), 156.4 (C-6a), 158.1 (C-8), 159.5 (C-2), 163.6 (*C*O$_2$Et). HRMS (ESI^+): m/z calcd for $[C_{16}H_{13}NO_5+H]^+$ 300.0872, found: 300.0851. Anal. Calcd. for $C_{16}H_{13}NO_5$: C 64.21, H 4.38, N 4.68. Found: C 64.41, H 4.44, N 4.85%.

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39. *Ethyl 4-methyl-2,8-dioxo-2H,8H-pyrano[2,3-f]chromene-9-carboxylate* **11**. A solution of ethyl 8-imino-4-methyl-2-oxo-2*H*,8*H*-pyrano[2,3-*f*]chromene-9-carboxylate **4d** (2.99 g, 0.01 mol) with acid HCl 4 N (10 mL) was stirred about 9 min under MW irradiation at 300 W. After reaction completion the precipitate was filtrated and washed with water to afford pure product **11**. Yield: 88%; mp. 255 °C; UV (λ): 305 cm^{-1}; IR (□, cm^{-1}): 3086, 1781, 1741, 1621, 1390, 1121, 1027; ^{1}H NMR (DMSO-d_6): δ 1.36 (t, 3H, *J* = 7.3 Hz, CH_2CH_3), 2.48 (s, 3H, 4-C*H*$_3$), 4. 35(q, 2H, *J* = 7.3 Hz, C*H*$_2$CH$_3$), 6.49 (s, 1H, H-3), 8.11 (d, 1H, *J* = 9.0 Hz, H-5), 7.44 (d, 1H *J* = 9.0 Hz, H-6), 8.77 (s, 1H, H-10); ^{13}C NMR (DMSO-d_6): δ 14.0 (CH_2CH_3), 18.3 (4-*C*H$_3$), 61.6 (*C*H$_2$CH$_3$), 106.8 (C-10a), 112.3 (C-6), 113.3 (C-3), 115.6 (C-4a), 117.6 (C-9), 131.0 (C-5), 141.0 (C-10), 150.3 (C-10b), 153.4 (C-4), 155.0 (C-6a), 156.1 (C-8), 158.5 (C-2), 161.9 (*C*O$_2$Et). HRMS (ESI^+): m/z calcd for $[C_{16}H_{12}O_6+Na]^+$ 323.0532, found: 323.0543. Anal. Calcd. for $C_{16}H_{12}O_6$: C 64.00, H 4.03. Found: C 64.20, H 4.12%.