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Microwave-Assisted Synthesis of 8-Aryl-10-chloro-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehydes and Their Antimicrobial Activity[1]

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Abstract—A series of new coumarin–chromene hybrids have been synthesized by conventional and microwave irradiation methods from 8-aryl-4-methyl-8,9-dihydropyrano[2,3-*f*]chromene-2,10-diones using the Vilsmeier–Haack reagent. All the synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS, and elemental analyses and were screened for antibacterial and antifungal activity. Among the compounds tested, methoxy-substituted pyranochromenones revealed the best antimicrobial profile.

Keywords: Coumarin, chromene, chromenecarbaldehyde, pyranochromene, Vilsmeier–Haack reaction

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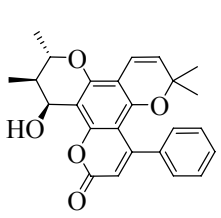
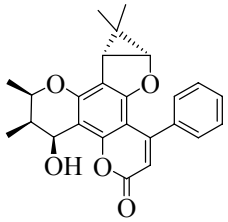
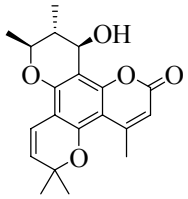
The coumarin and chromene moieties are important six-membered oxygen heterocyclic motifs embedded in several natural products and drugs. These systems are widely distributed in nature, and their derivatives have been shown to exhibit significant pharmacological activities [1]. Chromenes and fused chromenes are biologically important compounds due to their antibacterial [2], antifungal [3], antitumor [4], and antiviral [5] activity. Coumarin derivatives have been reported to exhibit antiinflammatory [6, 7], antimicrobial [8], antioxidant [9], anticancer [10], and chemoprophylactic [11] activities. Hybrid compounds containing both coumarin and chromene moieties, called pyranochromenones, may exhibit good biological activity due to combined effect. Patil et al. [12] reported that such pyranochromenone derivatives as Soulattrolide, Inophyllum G-1, Cordatolide A, and Oblongulide are potential anti-HIV agents.



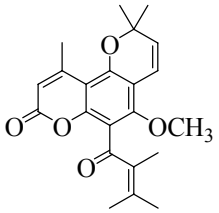
Soulattrolide



Inophyllum G-1



Cordatolide A



Oblongulide

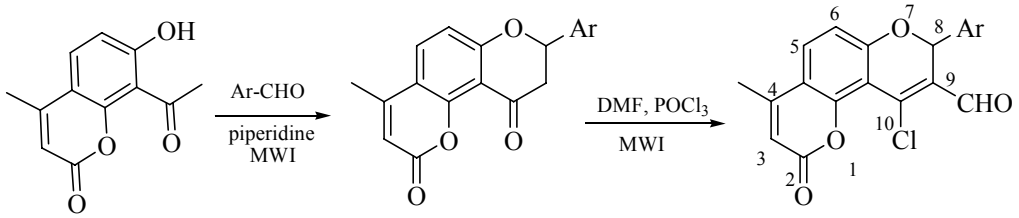
Microwave irradiation is known to provide enhanced reaction rate and improved product yield in chemical syntheses and is quite successful in the formation of a variety of carbon–heteroatom bonds. In recent years, microwaves have been extensively used for carrying out chemical reactions and have become a useful non-conventional energy source for performing organic syntheses [13, 14].

We reported previously on some 4-chlorochromenone derivatives which are potential biologically active compounds [15]. Encouraged by the pharmacological activities of pyranochromenones, we wish to report the synthesis of some new analogs by simple and convenient microwave irradiation method. Pyranochromenone derivatives **IIIa–IIIj** were synthesized from 8-acetyl-7-hydroxy-4-methyl-2*H*-chromen-2-one (**I**) and were screened for antimicrobial activity.

The synthetic route to compounds **IIIa–IIIj** is shown in Scheme 1. Compounds **IIa–IIj** were

[1] The text was submitted by the authors in English.

Scheme 1. Synthetic route for the preparation of pyranochromene derivatives **IIIa–IIIj**



I **IIa–IIj** **IIIa–IIIj**

For Ar, see Table 1.

synthesized as reported in [16]. The reaction of 8-acetyl-7-hydroxy-4-methylcoumarin with aromatic or heteroaromatic aldehydes in the presence of piperidine at room temperature gave the corresponding flavanones, 8-aryl-4-methyl-8,9-dihydropyrano[2,3-*f*]chromene-2,10-diones **IIa–IIj** which were brought into Vilsmeier–Haack reaction with DMF/$POCl_3$ [17] at room temperature to obtain 8-aryl-10-chloro-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehydes **IIIa–IIIj**. On the basis of spectral data, compound **IIIa** was identified as 10-chloro-4-methyl-2-oxo-8-phenyl-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde. The peak at 1078 cm^{-1} in the IR spectrum of **IIIa** confirmed the presence of C–O–C group, and the peak at 735 cm^{-1} confirmed the presence of chlorine. The signals at δ 6.44 ppm (8-H) in the ^1H NMR spectrum and at δ_C 73.2 (C^8) in the ^{13}C NMR spectrum of **IIIa** confirmed the formation of pyranochromenone skeleton. The base peak in the mass spectrum of **IIIa** appeared at *m*/*z* 353 due to $[M + H]^+$ ion.

The synthesis of 10-chloro-4-methyl-2-oxo-8-phenyl-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (**IIIa**) in multiSYNTH microwave system was optimized by varying irradiation power and reaction time. It was found that irradiation at a power of 100 W over a period of 5–6 min (Table 1) ensured the best yield of **IIIa**. The microwave-assisted reaction required a smaller amount of DMF than conventional method. Also, we compared the yields of the Vilsmeier–Haack reaction under both conventional heating and MW irradiation. In all cases, higher yields were obtained under MW irradiation (Table 1).

Newly synthesized compounds **IIIa–IIIj** (Table 2) were screened for their antibacterial activity against different types of bacterial strains (Figs. 1, 2), including Gram negative bacterial strains of *Escherichia coli* and *Pseudomonas aeruginosa* and Gram positive strains of *Staphylococcus aureus* and *Bacillus subtilis*, at a concentration of 100 μg/mL.

Table 1. Synthesis of pyranochromene derivatives **IIIa**–**IIIj**

Compound no.	Ar	Conventional heating		Microwave irradiation	
		time, h	yield, %	time, min	yield, %
IIIa	Ph	6	68	5	80
IIIb	4-$MeOC_6H_4$	6	65	6	82
IIIc	3,4-$(MeO)_2C_6H_4$	7	62	6	80
IIId	3,4,5-$(MeO)_3C_6H_4$	6	65	6	85
IIIe	2-ClC_6H_4	7	60	5	82
IIIf	4-MeC_6H_4	6	65	6	85
IIIg	4-BrC_6H_4	6	68	5	82
IIIh	4-*i*-PrC_6H_4	8	65	6	83
IIIi	4-FC_6H_4	6	64	6	86
IIIj	1-Naphthyl	8	62	6	80

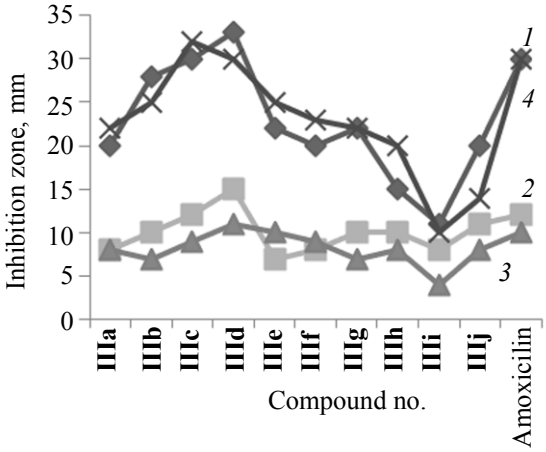


Fig. 1. Antibacterial activity against gram positive and gram negative bacterial strains: (*1*) *S. aureus,* (*2*) *B. subtilis,* (*3*) *P. Aeruginosa*, and (*4*) *E. coli.*

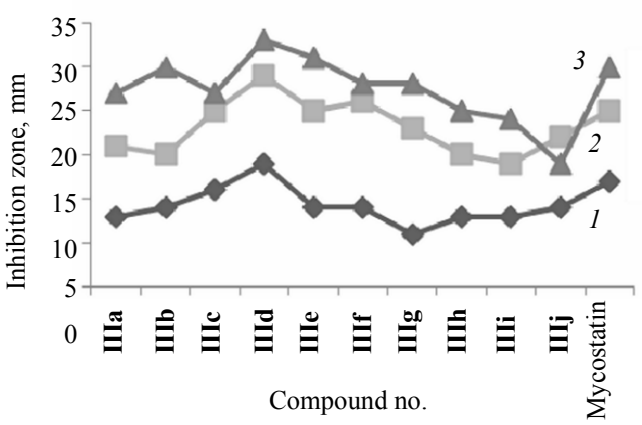


Fig. 2. Antifungal activity against pathogenic fungal strains: (*1*) *Aspergillus nigerzeae,* (*2*) *Penicillium italicum,* and (*3*) *Fusarium oxysporum.*

Compounds **IIIc** and **IIId** showed high activity against *Staphylococcus aureus*, and compounds **IIIb**–**IIId**, **IIIg**, **IIIh**, and **IIIj** showed better activity against *Bacillus subtilis* compared to standard drug *Amoxicilin* at a concentration of 100 μg/mL.

Among Gram negative bacterial strains, compounds **IIIc** and **IIId** showed high activity against *Escherichia coli*, and the antibacterial activity of **IIIa**, **IIIc**–**IIIf**, **IIIh**, and **IIIj** against *Pseudomonas aeruginosa* was comparable to that of *Amoxicilin*. It is seen that compounds **IIIc** and **IIId** exhibit a broad spectrum of antibacterial activity against all the tested strains.

The antifungal activity of compounds **IIIa**–**IIIj** was tested against three pathogenic fungi (Table 3), namely *Aspergillus nigerzeae*, *Pencillium italicum*, and *Fusarium oxysporum* at a concentration of 100 μg/mL using Mycostatin as reference drug. Compounds **IIIc** and **IIId** were highly active against *Aspergillus nigerzeae*, compounds **IIIc**–**IIIg** showed high activity against *Pencillium italicum*, and compounds **IIIb** and

Table 2. Antibacterial activity (inhibition zone, mm) of compounds **IIIa**–**IIIj** at a concentration of 100 μg/mL

Compound no.	Gram positive		Gram negative	
	S. aureus	*B. subtilis*	*P. aeruginosa*	*E. coli*
IIIa	20	8	8	22
IIIb	28	10	7	25
IIIc	30	12	9	32
IIId	33	15	11	30
IIIe	22	7	10	25
IIIf	20	8	9	23
IIIg	22	10	7	22
IIIh	15	10	8	20
IIIi	11	8	4	10
IIIj	20	11	8	14
Amoxicilin	30	12	10	30

Table 3. Antifungal activity (inhibition zone, mm) of compounds **IIIa**–**IIIj** at a concentration of 100 μg/mL

Compound no.	*Aspergillus nigerzeae*	*Penicillium italicum*	*Fusarium oxysporum*
IIIa	8	16	22
IIIb	9	15	25
IIIc	11	20	22
IIId	14	24	28
IIIe	9	20	26
IIIf	9	21	23
IIIg	6	18	23
IIIh	8	15	20
IIIi	8	14	19
IIIj	9	17	14
Mycostatin	12	20	25

IIId–IIIg showed high activity against *Fusarium oxysporum*. Compound **IIId** showed a broad spectrum of antifungal activity against all the tested strains.

In summary, we have synthesized a series of new 8-aryl-10-chloro-4-methyl-2-oxo-2,8-dihydropyrano-[2,3-*f*]chromene-9-carbaldehydes **IIIa–IIIj** by conventional and microwave irradiation methods. The reactions under microwave irradiation were completed in shorter time with better yields than under conventional conditions. Screening of the new compounds for antimicrobial and antifungal activity revealed broad spectrum of antibacterial activity of **IIIc** and **IIId** and broad spectrum of antifungal activity of **IIId**.

EXPERIMENTAL

All used materials were commercial products purchased mostly from Sigma Aldrich and were used without further purification. The melting points were determined in open capillaries and are uncorrected. The purity of the newly synthesized compounds was checked by TLC on silica gel 60 F254 (Merck). The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 spectrometer using tetramethylsilane as internal standard. The IR spectra were recorded in KBr on a Shimadzu FTIR 8400S spectrometer. The mass spectra were obtained on a Shimadzu GCMS-QP 1000 instrument. Microwave-assisted reactions were carried out in a Milestone multiSYNTH microwave system.

General procedures for the synthesis of 8-aryl-10-chloro-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]-chromene-9-carbaldehydes IIIa–IIIj. *a*. *Conventional method*. A round-bottom flask was charged with 5 mL of DMF and cooled to 0–5°C, 0.006 mol of phosphoryl chloride was added dropwise under stirring, the mixture was stirred for 15 min at 0 to 5°C, and a solution of 0.001 mol of 8-aryl-4-methyl-8,9-dihydropyrano[2,3-*f*]chromene-2,10-dione **IIa–IIj** in 3 mL of DMF was added. The mixture was stirred for 30 min at 0 to 5°C and for 6 to 8 h at room temperature (Table 1). When the reaction was complete (TLC, EtOAc–hexane, 1 : 3 by volume), the mixture was poured into ice water, neutralized with 10% aqueous NaOH, and extracted with chloroform. The combined extracts were washed with water and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel column chromatography to afford pure product **IIIa–IIIj**.

b. *Microwave-assisted reaction.* A round-bottom flask was charged with 2 mL of DMF and cooled to 0–5°C, 0.006 mol of phosphoryl chloride was added dropwise under stirring, the mixture was stirred for 15 min at 0 to 5°C, and a solution of 0.001 mol of 8-aryl-4-methyl-8,9-dihydropyrano[2,3-*f*]chromene-2,10-dione **IIa–IIj** in 2 mL of DMF was added. The mixture was maintained for 30 min at 0 to 5°C and was then irradiated in a multiSYNTH microwave furnace at 100 W over a period indicated in Table 1. When the reaction was complete (TLC, EtOAc–hexane, 1 : 3 by volume), the mixture was poured into ice water, neutralized with 10% aqueous NaOH, and extracted with chloroform. The combined extracts were washed with water and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel column chromatography to afford pure product **IIIa–IIIj**.

10-Chloro-4-methyl-2-oxo-8-phenyl-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIa). Yield 80%, mp 198–200°C. IR spectrum, ν, cm^{-1}: 737 (C–Cl), 1078 (C–O–C), 1745 (CH=O). ^{1}H NMR spectrum, δ, ppm: 2.31 d (3H, CH_3, J = 1.004 Hz), 5.98 d (1H, 3-H, J = 1.004 Hz), 6.52 s (1H, 8-H), 6.98 d (1H, 6-H, J = 8.78 Hz,), 7.27–7.36 m (5H, H_{arom}), 7.54 d (1H, 5-H, J = 8.78 Hz), 9.66 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 18.9 (CH_3), 73.2 (C^8), 112.3, 114.1, 114.9, 126.8, 128.5, 128.6, 129.0, 130.1, 137.4, 147.6, 151.9, 152.2, 157.9, 158.6, 162.0, 164.5 (C=O), 190.1 (CHO). Mass spectrum: m/z 353 $[M + H]^+$. Found, %: C 68.14; H 3.76; $C_{20}H_{13}ClO_4$. Calculated, %: C 68.09; H 3.71.

10-Chloro-8-(4-methoxyphenyl)-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIb). Yield 82%, mp 206–208°C. IR spectrum, ν, cm^{-1}: 737 (C–Cl), 1088 (C–O–C), 1725 (CH=O). ^{1}H NMR spectrum, δ, ppm: 2.38 d (3H, CH_3, J = 1.004 Hz), 3.80 s (3H, OCH_3), 6.11 d (1H, 3-H, J = 1.004 Hz), 6.18 s (1H, 8-H), 6.85 d (1H, 6-H, J = 8.78 Hz), 6.89 d (2H, H_{arom}, J = 8.55 Hz), 7.38 d (2H, H_{arom}, J = 8.55 Hz), 7.46 d (1H, 5-H, J = 8.78 Hz), 9.89 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.0 (CH_3), 55.3, 78.4 (C^8), 109.6, 112.3, 113.3, 114.1 114.9, 124.6, 125.5, 126.4, 129.0, 129.8, 150.2, 152.3, 157.3, 160.0, 160.2 (C=O), 192.8 (CHO). Found, %: C 65.93; H 3.98. $C_{21}H_{15}ClO_5$. Calculated, %: C 65.89; H 3.95. Mass spectrum: m/z 383 $[M + H]^+$.

10-Chloro-8-(3,4-dimethoxyphenyl)-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIc). Yield 80%, mp 190–192°C. IR spectrum,

ν, cm^{-1}: 739 (C–Cl), 1086 (C–O–C), 1725 (CH=O). ^1H NMR spectrum, δ, ppm: 2.38 d (3H, CH_3, J = 1.004 Hz), 3.87 s and 3.89 (s (3H each, OCH_3), 5.78 s (1H, 8-H), 6.19 d (1H, 3-H, J = 1.004 Hz), 6.84 d (1H, 6-H, J = 8.78 Hz), 6.85–7.26 m (3H, H_{arom}), 7.46 d (1H, 5-H, J = 8.78 Hz), 9.49 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.02 (CH_3), 55.9, 56.0, 77.9 (C^8), 109.6, 110.4, 112.3, 113.2, 114.9, 120.2, 124.6, 125.5, 126.5, 130.1, 149.1, 149.6, 150.2, 152.5, 157.2, 160.0 (C=O), 190.2 (CHO). Found, %: C 64.05; H 4.19. $C_{22}H_{17}ClO_6$. Calculated, %: C 64.01; H 4.15. Mass spectrum: m/z 413 $[M + H]^+$.

10-Chloro-4-methyl-2-oxo-8-(3,4,5-trimethoxyphenyl)-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIId). Yield: 85%, mp 206–208°C. IR spectrum, ν, cm^{-1}: 741 (C–Cl), 1088 (C–O–C), 1727 (CH=O). ^1H NMR spectrum, δ, ppm: 2.38 d (3H, CH_3, J = 1.004 Hz), 3.80 s (3H, OCH_3), 3.84 s (6H, OCH_3), 6.22 d (1H, 3-H, J = 1.004 Hz), 6.42 s (1H, 8-H), 7.23 d (1H, 6-H, J = 8.78 Hz), 7.37 s (2H, H_{arom}), 7.52 d (1H, 5-H, J = 8.78 Hz), 10.42 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.3 (CH_3), 54.6, 56.2, 76.8 (C^8), 110.5, 112.7, 113.2, 114.6, 121.4, 123.6, 126.5, 132.4, 148.9, 149.6, 150.2, 152.5, 160.0, 162.2 (C=O), 190.5 (CHO). Found, %: C 62.42; H 4.36. $C_{23}H_{19}ClO_7$. Calculated, %: C 62.38; H 4.32. Mass spectrum: m/z 443 $[M + H]^+$.

10-Chloro-8-(2-chlorophenyl)-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIe). Yield 82%, mp 182–184°C. IR spectrum, ν, cm^{-1}: 751 (C–Cl), 1074 (C–O–C), 1736 (CH=O). ^1H NMR spectrum, δ, ppm: 2.37 d (3H, CH_3, J = 1.004 Hz), 6.23 d (1H, 3-H, J = 1.004 Hz), 6.83 s (1H, 8-H), 6.84 d (1H 6-H, J = 8.78 Hz), 7.07–7.44 m (4H, H_{arom}), 7.53 d (1H, 5-H, J = 8.78 Hz), 10.36 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.3 (CH_3), 73.7 (C^8), 112.7, 114.0, 115.2, 120.2, 122.3, 122.9, 124.5, 126.9, 128.6, 129.0, 129.1, 129.6, 134.4, 136.1, 152.4, 158.4, 159.3, 162.3 (C=O), 188.8 (CHO). Found, %: C 62.07; H 3.16. $C_{20}H_{12}Cl_2O_4$. Calculated, %: C 62.04; H 3.12. Mass spectrum: m/z 387 $[M + H]^+$.

10-Chloro-4-methyl-8-(4-methylphenyl)-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIf). Yield 85%, mp 200–202°C. IR spectrum, ν, cm^{-1}: 739 (C–Cl), 1084 (C–O–C), 1728 (CH=O). ^1H NMR spectrum, δ, ppm: 2.34 s (3H, CH_3, J = 1.004 Hz), 2.36 s (3H, C**H**$_3C_6H_4$), 6.01 d (1H, 3-H, J = 1.004 Hz), 6.22 s (1H, 8-H), 7.18 d (1H, 6-H, J = 8.78 Hz), 7.48 d (2H, H_{arom}, J = 8.53 Hz), 7.76 d (2H, H_{arom}, J = 8.53 Hz), 7.92 d (1H, 5-H, J = 8.78 Hz), 9.63 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.0 (CH_3), 21.2, 77.8 (C^8), 112.3, 113.2, 124.6, 125.4, 126.2, 126.4, 127.3, 129.1, 129.5, 129.8, 134.9, 139.0, 152.9, 157.3, 160.0 (C=O), 190.3 (CHO). Found, %: C 68.80; H 4.15. $C_{21}H_{15}ClO_4$. Calculated, %: C 68.76; H 4.12. Mass spectrum: m/z 367 $[M + H]^+$.

8-(4-Bromophenyl)-10-chloro-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIg). Yield 82%, mp 204–206°C. IR spectrum, ν, cm^{-1}: 735 (C–Cl), 1076 (C–O–C), 1738 (CH=O). ^1H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3, J = 1.004 Hz), 6.07 d (1H, 3-H, J = 1.004 Hz), 6.23 s (1H, 8-H), 6.86 d (1H, 6-H, J = 8.78 Hz), 6.95 d (2H, H_{arom}, J = 8.56 Hz), 6.97 d (2H, H_{arom}, J = 8.56 Hz), 7.47 d (1H, 5-H, J = 8.78 Hz), 9.63 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.3 (CH_3), 73.7 (C^8), 112.7, 114.0, 115.2, 120.2, 122.3, 122.9, 124.5, 126.9, 128.6, 129.0, 129.1, 129.6, 134.4, 136.1, 152.4, 158.4, 159.3 (C=O), 188.8 (CHO). Found, %: C 55.68; H 2.83. $C_{20}H_{12}BrClO_4$. Calculated, %: C 55.65; H 2.80. Mass spectrum: m/z 431 $[M + H]^+$.

10-Chloro-8-(4-isopropylphenyl)-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIh). Yield 83%, mp 166–168°C. IR spectrum, ν, cm^{-1}: 750 (C–Cl), 1088 (C–O–C), 1725 (CH=O). ^1H NMR spectrum, δ, ppm: 1.46 s (6H, CH_3) 2.38 d (3H, J = 1.004 Hz), 2.45 m [1H, C**H**$(CH_3)_2$], 6.08 d (1H, 3-H, J = 1.004 Hz), 6.54 s (1H, 8-H), 6.87 d (1H, 6-H, J = 8.78 Hz), 7.25–7.27 d (2H, H_{arom}, J = 8.64), 7.32 d (2H, J = 8.64 Hz), 7.54 d (1H, 5-H, J = 8.78 Hz), 10.36 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 13.2 [CH(**C**$H_3)_2$], 19.0 (CH_3), 25.3 [**C**H$(CH_3)_2$], 76.4 (C^8), 112.3, 113.9, 120.3, 121.2, 122.2, 123.8, 124.6, 125.5, 126.4, 129.0, 129.8, 150.2, 152.3, 157.3, 160.2 (C=O), 190.2 (CHO). Found, %: C 69.96; H 4.85. $C_{23}H_{19}ClO_4$. Calculated, %: C 69.92; H 4.81. Mass spectrum: m/z 395 $[M + H]^+$.

10-Chloro-8-(4-fluorophenyl)-4-methyl-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIi). Yield 86%, mp 200–202°C. IR spectrum, ν, cm^{-1}: 745 (C–Cl), 1078 (C–O–C), 1740 (CH=O). ^1H NMR spectrum, δ, ppm: 2.36 d (3H, CH_3, J = 1.004 Hz), 5.80 d (1H, 3-H, J = 1.004 Hz), 6.18 s (1H, 8-H), 6.81 d (1H, 6-H, J = 8.78), 6.89 d (2H, H_{arom}, J = 8.72), 7.31 d (2H, H_{arom}, J = 8.72 Hz), 7.43 d (1H, 5-H, J = 8.78 Hz), 9.59 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.3 (CH_3), 73.7 (C^8), 112.7, 114.0, 115.2, 120.2, 122.3, 122.9, 124.5, 126.9, 128.6, 129.0, 129.1, 129.6, 134.4, 136.1, 152.4, 158.4, 159.3, 160.2 (C=O), 190.5 (CHO).

Found, %: C 64.82; H 3.30. $C_{20}H_{12}ClFO_4$. Calculated, %: C 64.79; H 3.26. Mass spectrum: *m*/*z* 371 $[M + H]^+$.

10-Chloro-4-methyl-8-(naphthalen-1-yl)-2-oxo-2,8-dihydropyrano[2,3-*f*]chromene-9-carbaldehyde (IIIj). Yield 80%, mp 205–207°C. IR spectrum, ν, cm^{-1}: 756 (C–Cl), 1076 (C–O–C), 1745 (CH=O). ^1H NMR spectrum, δ, ppm: 2.31 d (3H, CH_3, J = 1.004 Hz), 6.20 d (1H, 3-H, J = 1.004 Hz), 6.68 d (1H, 6-H, J = 8.78 Hz), 7.23 s (1H, 8-H), 7.39–7.78 m (5H, H_{arom}), 7.84 d (1H, 5-H, J = 8.78 Hz), 8.13–8.56 m (2H, H_{arom}), 10.45 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 19.1 (CH_3), 74.7 (C^8), 112.7, 114.0, 115.2, 120.2, 121.2, 121.6, 122.3, 122.9, 123.4, 124.5, 126.9, 128.6, 129.0, 129.1, 129.6, 136.1, 152.4, 158.4, 159.3 (C=O), 188.8 (CHO). Found, %: C 71.61; H 3.79. $C_{24}H_{15}ClO_4$. Calculated, %: C 71.56; H 3.75. Mass spectrum: *m*/*z* 403 $[M + H]^+$.

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REFERENCES

1. Cassidy, F., Evans, J.M., Hadley, M.S., Haladij, A.H., Leach, P.E., and Stemp, G.. *J. Med. Chem*., 1992, vol. 35, p.1623.
2. El-Agrody, A.M., El-Hakim, M.H., AbdEl-Latif, M.S., Fakery, A.H., El Sayeed, and Ghareeb, El-K.A., *Acta Pharm*., 2000, vol. 50, p. 111.
3. Ohira, T. and Yatagai, M., *J. Jpn. Wood Res. Soc*., 1993, vol. 39, p. 231.
4. Mohr, S.J., Chirigos, M.A., Fuhrman, F.S., and Pryor, J.W., *Cancer Res*., 1975, vol. 35, p.3750.
5. Martinez, A.G. and Marco, L.J., *Bioorg. Med. Chem. Lett*., 1997, vol. 24, p.3165.
6. Jung, K., Park, Y.J., and Ryu, J.S., *Synth. Commun*., 2008, vol. 38, p. 4395.
7. Kaczka, E.A., Wolf, F.J., Ratha, F.P., and Folkers, K.J., *J. Am. Chem. Soc*., 1955, vol. 77, p. 6404.
8. Mulwad, V.V. and Shirodkhar, J.M., *Indian J. Heterocycl. Chem*., 2002, vol.11, p. 192.
9. Kusanur, R., Manjunath, G., and Kulkarni, M.V., *Indian J. Heterocycl. Chem*., 2004, vol. 13, p. 201.
10. Rajeshwar Rao, V., Srimanth, K., and Vijaya Kumar, P., *Indian J. Heterocycl. Chem*., 2004, vol. 14, p. 141.
11. Nofal, Z.M., El-Zahar, M.I., and Abd El-Karim, S.S., *Egypt. J. Chem*., 2005, vol. 48 p. 587.
12. Patil, A.D., Freyer, A.J., Eggleston, D.S., Haltiwanger, R.C., Bean, M.F., Taylor, P.B., Caranfa, M.J., Breen, A.L., Bartus, H.R., Johnson, R.K., Hertzberg, R.P., and Westley, J.W., *J. Med. Chem*., 1993, vol. 36, p. 4131.
13. Gedye, R.N. and Wei, J.B., *Can. J. Chem*., 1998, vol. 76, p. 525.
14. Varma, R.S., *Green Chem*., 1999, vol. 1, p. 43.
15. Ashok, D., Sudershan, K., and Khalilullah, M., *Indian J. Heterocycl. Chem*., 2012, vol. 21, p. 301.
16. Chand, K., Amir, N.S., Preethi, Y., Rmesh, K., Tiwari, K., Meena, K., Keykavous, P. and Sunil, K.S., *Can. J. Chem*., 2013, vol. 91, p. 741.
17. Venkati, M., Satyanarayana Reddy, S., Swamy, G.Y.S.K., Ravikumar, K., and Krupadanam, G.L.D., *Arkivoc*, 2012, part (vi), p. 355.
18. Benson, H.J., *Microbiological Applications: A Laboratory Manual in General Microbiology*, Dubuque, Iowa: W.C. Brown, 1990, 5th ed.