DESIGN, SYNTHESIS AND STRUCTURAL EVALUATION OF 6-C- METHYLATED HOMOISOFLAVONES AND ITS DERIVATIVES

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Abstract:
The synthesis of twelve new 6-*C*-methylated homoisoflavones from dihydrochalcones using PCl_5/DMF complex.

Keywords: 6-*C*-methylated homoisoflavones, dihydrochalcones, PCl_5/DMF complex.

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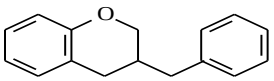
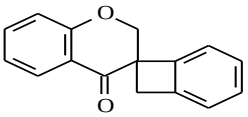
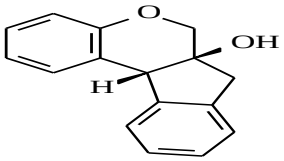
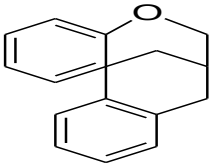
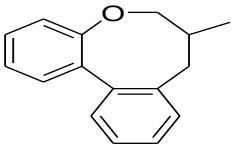
Introduction

Nature produces a myriad of chemicals and natural products in its quest to sustain and propagate life. Homoisoflavonoids, a rare class of natural compounds comprises naturally occurring oxygen heterocyclic compounds. They play a special role in the field of heterocycles as this skeleton is an integral part of many natural products. And these compounds belongs to the family of natural plant metabolites which differ from that of isoflavanoids by the **presence of an extra carbon atom[1-3].**

Homoisoflavonoids are an uncommon subclass of flavonoids which were also structurally related to the more prevalent flavonoids occurs predominantly in the Liliaceae[4-7,13,15,20,23-29,31,32,35-37,39,40,42,43,50-52], Leguminosae[8-12,16,17,19,30,34,45-49], Hyacinthaceae[14,33,38,41], Fabaceae, Asparagaceae, Polygonaceae, Portulaceae, Orchidaceae, Gentianaceae, Agavaceae[22] and Ruscaceae[18] families.

Presently, approximately 240 naturally occurring homoisoflavonoids have been identified despite of their rare occurrence in nature,[57,58] according to their structural traits. According to the literature survey, the homoisoflavonoids isolated so far could be classified into five types based on their carbon skeleton: Sappanin-type, Scillascillin-type, Brazilin -type, Caesalpin-type and Protosappanin-type (**Table 1)**.

Table 1: Types of homoisoflavonoids

S. No	Types of homoisoflavonoids	Structure
1.	Sappanin-type compounds	
2.	Scillascillin type compounds	
3.	Brazilin type compounds	
4.	Cesalpin type compounds	
5.	Proto-sappanin type compounds	

Homoisoflavanoids display a wide spectrum of biological activities. Several natural and synthetic homoisoflavonoids shows a multiple biomedical properties such a anti-fungal,[54] anti-viral,[55,56,59] anti-mutagenic,[12,60] anti-proliferative,[61] anti-oxidant,[53,62] anti-allergic, anti-histaminic,[60] anti-inflammatory,[63] protein tyrosine kinase (PTK) inhibitor activity,[64] cough relief,[65] angio protective,[66] inhibition of platelet aggregation activity,[67] phosphidiesterase isoenzyme-inhibiting,[74] monoamine oxidase and choline sterase inhibitor activities.[68,69]

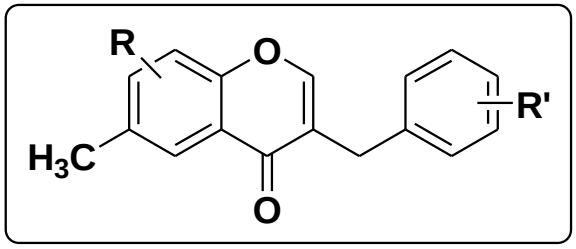
Homoisoflavonoids (3-benzylidenechroman-4-ones) are well known natural products possessing a diverse pharmacological properties related to AD, such as anti-AChE activity,[70] Ab fibril formation inhibitory activity,[71] MAO-B inhibitory effect,[67] neuroprotection capability[72] and anti-diabetic activity.[18,73] And these compounds known to act as a growth inhibitors of the sporogeneses and the enzymes involved in the infection mechanism of *Phytophthora parasitica.*[75]

On the other hand, various 3-benzyl-chromones possess angio protective, anti-allergic, anti-

histaminic properties.[76] Their properties turn homoisoflavonoids a very interesting targets to organic chemists.

Results and Discussion

On a thorough study on homoisoflavanoids, it was came to know that an intense research was going on isolation, synthesis and applications of homoisoflavanoids and their derivatives. In glance of attracting biological activities, the author got her attention to synthesize various 6-*C*-methylated homoisoflavones which are not focused well in literature.



6-*C*-Methylated homoisoflavone

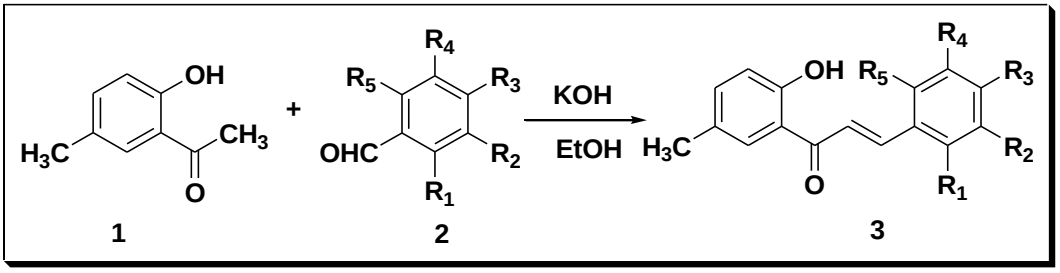
The 6-*C*-methylated homoisoflavones were synthesized from the dihydrochalcones by adopting the following general methodology. The dihydrochalcones have been prepared by the reduction of the chalcones, which were prepared from readily available 2-hydroxy acetophenones and aldehydes in the presence of base. The method consists of three major steps which were given below.

1. Synthesis of 5-*C*-methylated chalcones from 5-*C*-methylated acetophenones and aromatic aldehydes in the presence of base.

2. Synthesis of 5-*C*-methylated dihydrochalcones by the reduction of corresponding chalcones.

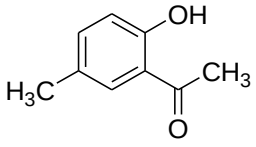
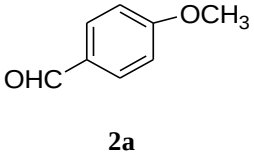
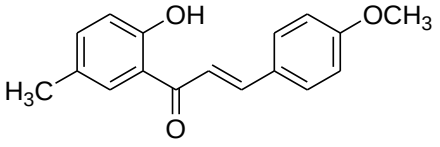
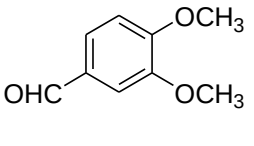
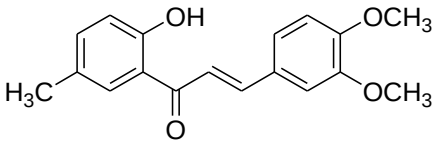
3. Synthesis of target compounds by the reaction of 5-*C*-methylated dihydrochalcones with N, N′-dimethyl(chloromethylene)ammonium chloride generated *in situ* from DMF and PCl_5 for one carbon extension at about room temperature to afford 6-*C*-methylated homoisoflavones.

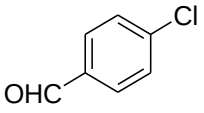
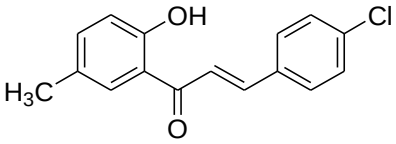
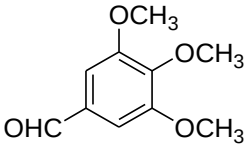
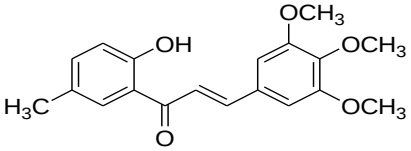
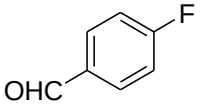
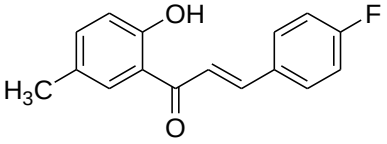
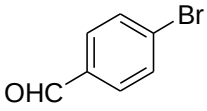
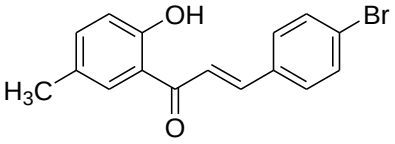
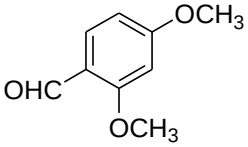
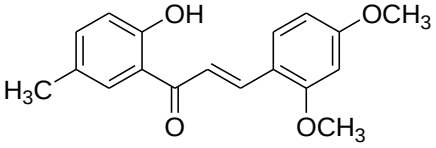
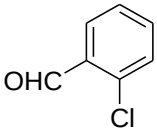
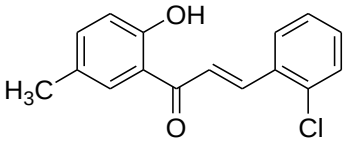
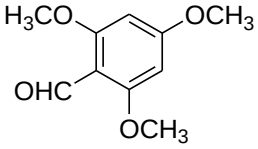
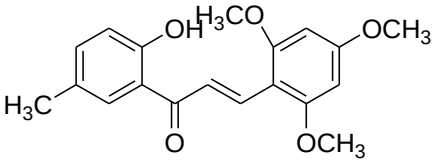
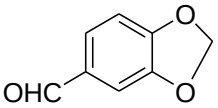
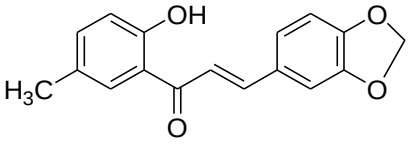
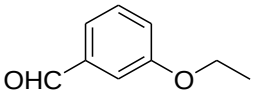
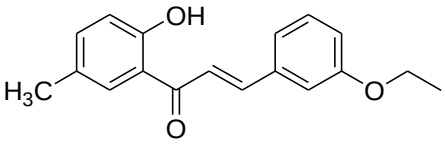
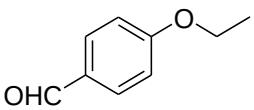
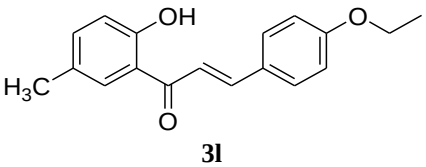
SYNTHESIS OF CHALCONES (3a-3l):
The desired chalcones (**3a-3l**) were prepared by the condensation
of 2-hydroxy-5-methyl acetophenone (**1**) with substituted benzaldehydes **(2)** in the presence of strong base (KOH) in ethanol at room temperature as shown in (**Scheme-1)**.



Scheme 1: Synthesis of chalcones

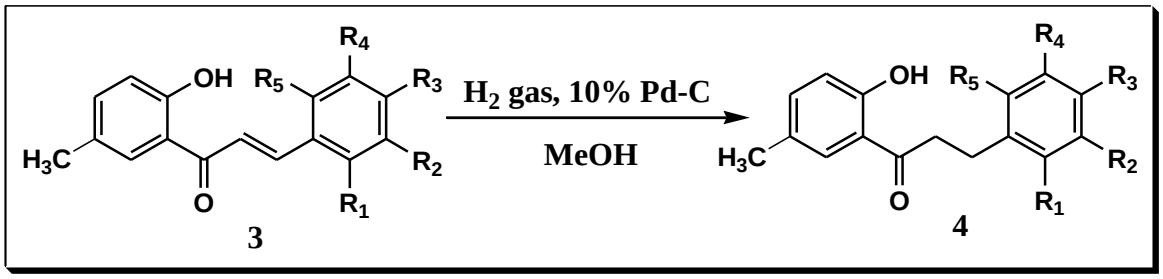
Table 2: Synthesis of chalcones

S. No	1	2	Product 3	Yield (%)
1.	 **1a**	 **2a**	 **3a**	82
2.	**1a**	 **2b**	 **3b**	79

3.	**1a**	 **2c**	 **3c**	78
4.	**1a**	 **2d**	 **3d**	88
5.	**1a**	 **2e**	 **3e**	76
6.	**1a**	 **2f**	 **3f**	75
7.	**1a**	 **2g**	 **3g**	80
8.	**1a**	 **2h**	 **3h**	78
9.	**1a**	 **2i**	 **3i**	74
10.	**1a**	 **2j**	 **3j**	86
11.	**1a**	 **2k**	 **3k**	80
12.	**1a**	 **2l**	 **3l**	82

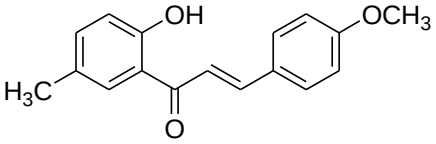
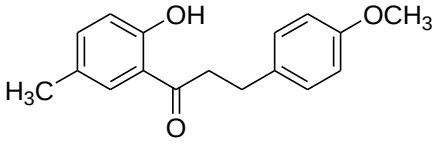
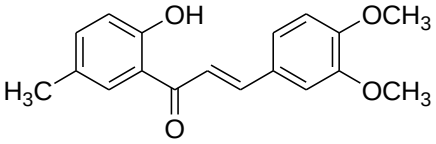
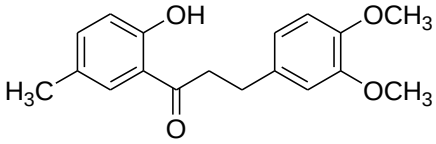
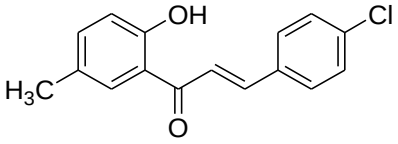
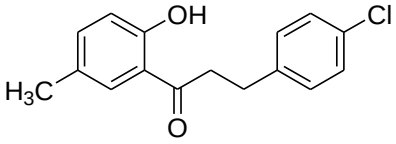
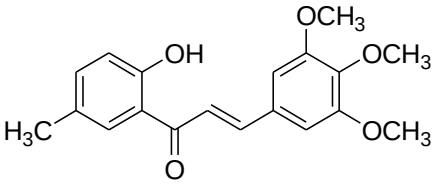
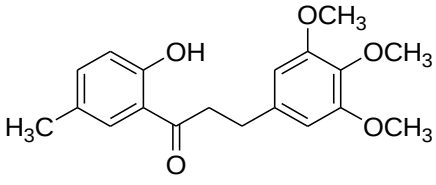
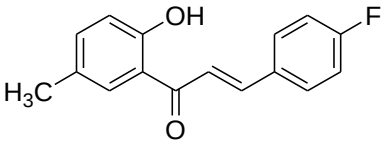
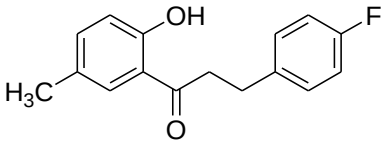
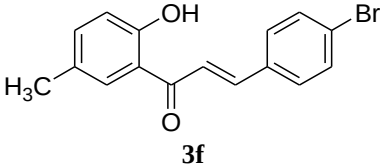
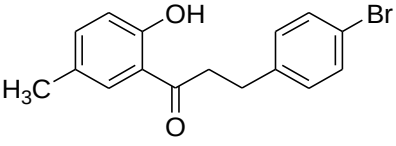
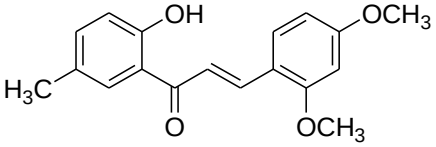
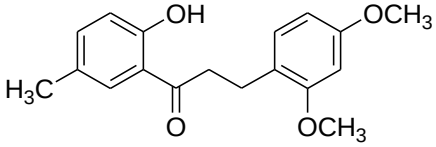
SYNTHESIS OF DIHYDROCHALCONE (4a-4l):

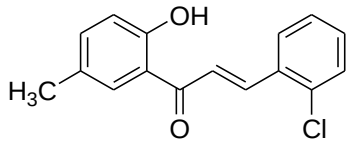
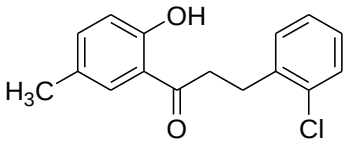
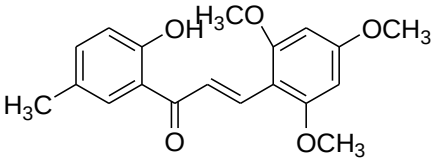
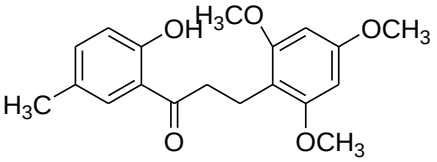
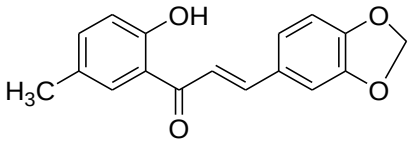
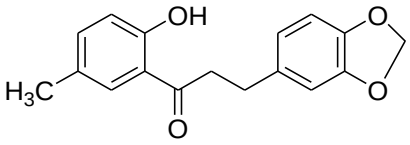
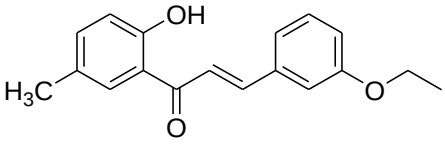
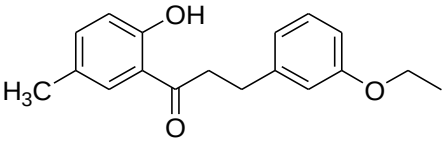
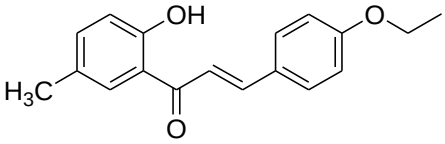
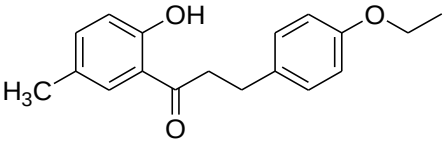
The desired dihydrochalcones **(4a-4l)** were prepared from chalcones (**3a-3l**) in methanol by passing hydrogen gas in presence of 10 % Pd-C at room temperature as shown in (**Scheme 2)**.



Scheme 2: Synthesis of dihydrochalcones

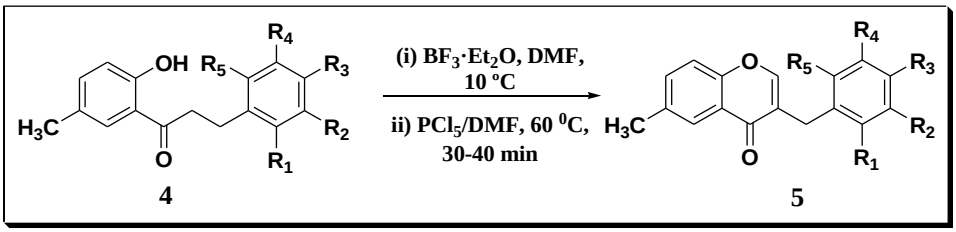
Table 3: Synthesis of dihydrochalcones

S. No	3	4	Yield(%)
1.	 **3a**	 **4a**	76
2.	 **3b**	 **4b**	82
3.	 **3c**	 **4c**	78
4.	 **3d**	 **4d**	73
5.	 **3e**	 **4e**	75
6.	 **3f**	 **4f**	70
7.	 **3g**	 **4g**	78

8.	 **3h**	 **4h**	73
9.	 **3i**	 **4i**	77
10.	 **3j**	 **4j**	79
11.	 **3k**	 **4k**	70
12.	 **3l**	 **4l**	75

SYNTHESIS OF 6-*C*-METHYLATED HOMOISOFLAVONES (5a-5l):

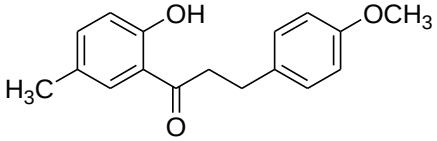
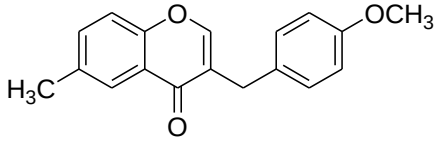
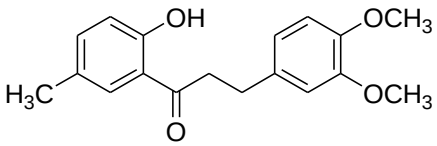
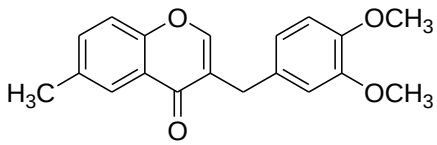
The desired 6-*C*-methylated homoisoflavones **(5a-5l)** were prepared from the corresponding dihydrochalcones **(4a-4l)** by one carbon-extension using $BF_3{\cdot}Et_2O$, DMF and PCl_5/DMF complex as shown in (**Scheme 3)**.

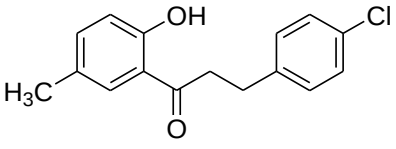
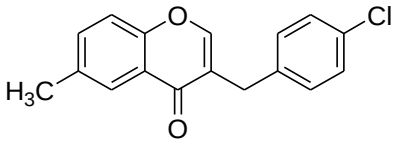
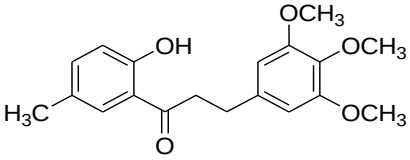
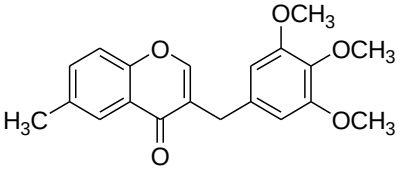
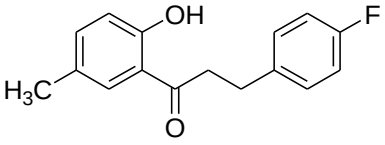
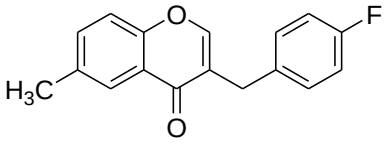
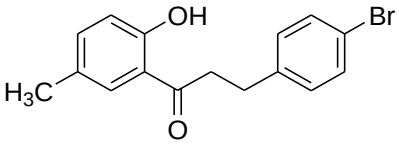
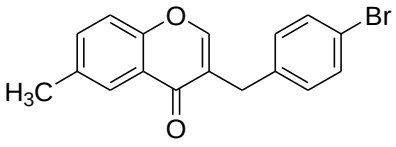
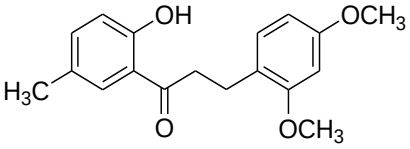
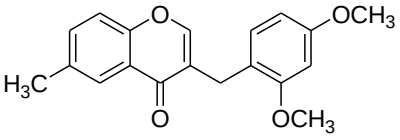
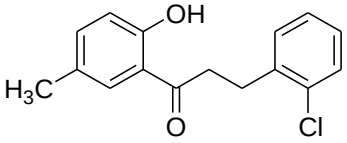
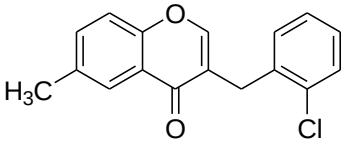
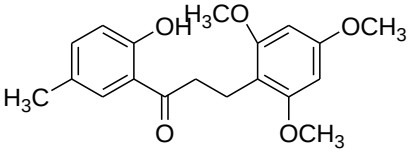
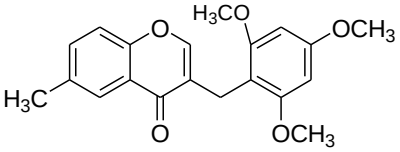
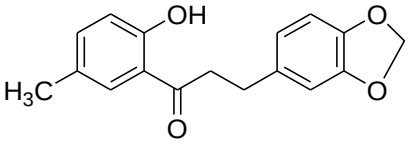
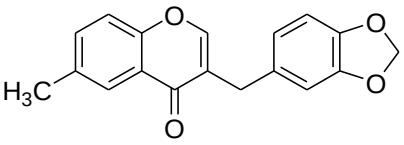
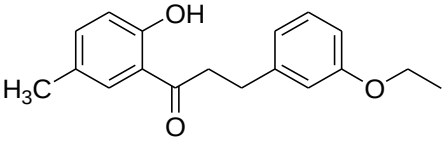
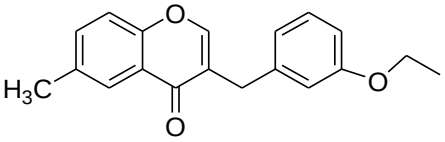
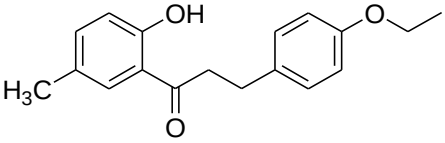
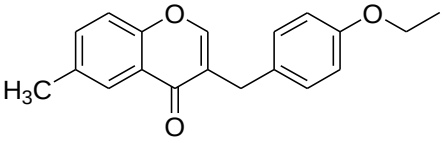


4 **5**

Scheme 3: Synthesis of 6-*C*-methylated homoisoflavones

Table 4: Synthesis of 6-*C*-methylated homoisoflavones

S. No	4	5	Yield(%)
1.	 **4a**	 **5a**	78
2.	 **4b**	 **5b**	80

3.	 **4c**	 **5c**	72
4.	 **4d**	 **5d**	74
5.	 **4e**	 **5e**	80
6.	 **4f**	 **5f**	75
7.	 **4g**	 **5g**	72
8.	 **4h**	 **5h**	68
9.	 **4i**	 **5i**	70
10.	 **4j**	 **5j**	65
11.	 **4k**	 **5k**	71
12.	 **4l**	 **5l**	75

Conclusion

Up to now only naturally occurring 6-*C*-methylated homoisoflavones are observed, from the known method the author synthesized a series of twelve new 6-*C*-methylated homoisoflavones from dihydrochalcones using PCl_5/DMF complex. She

believes that the present method could be of wide application in medicinal chemistry and organic chemistry. And the research on their biological activities are in progress.

Acknowledgments
The author, Sarakula Prasanthi thank the University Grants Commision (UGC), New Delhi for financial assistance through the Rajiv Gandhi National Fellowship (RGNF). The author is also greatful to the Department of Organic Chemistry & FDW, Andhra University, Visakhapatnam, Andhra Pradesh for providing the facilities to carry out research work.

EXPERIMENTAL SECTION

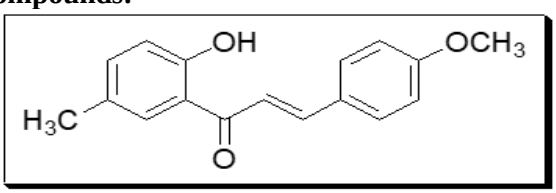
Materials & Methods

All synthesized compound melting points were recorded on a Mel-Temp melting point apparatus in open capillaries and are uncorrected. IR spectra were recorded on a Perkin-Elmer BX1 FTIR spectrophotometer and ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AMX 400 MHz NMR spectrometer using TMS as the internal standard and the values for chemical shifts (δ) being given in parts per million and coupling constants (*J*) in hertz. Mass spectra were recorded on an Agilent1100 LC/MSD. Acme silica gel G and silica gel (100–200 mesh) were used for analytical thin-layer chromatography and column chromatography, respectively.

General procedure for the preparation of chalcone (3a-3l):

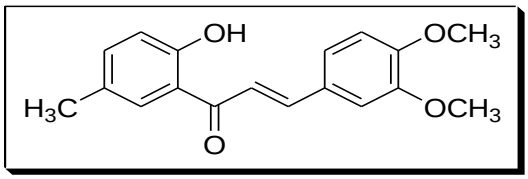
To a solution of 2-hydroxy-5-methyl acetophenone **(1)** (6 mmol) and substituted benzaldehyde **(2)** (6 mmol) in 10 mL ethanol, aqueous KOH (6 mmol) was added. The reaction mixture was stirred for 24 h at room temperature. After completion of the reaction, ice cold water was added to the reaction mixture to get a yellow colour solid. The solid was filtered and dissolved in ethyl acetate and dried over sodium sulphate and concentrated under vacuum.

Characterization data of all synthesized compounds:



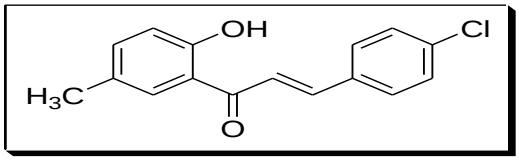
3a

2-Hydroxy-5-methyl-4′-methoxychalcone (3a): Mp: 102-104 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 3.84 (s, 3H, OCH_3 at C-3′), 6.88 (d, *J* = 7.6 Hz, 1H, H-3), 6.93 (d, *J* = 8.0Hz, 2H, H-3′, 5′), 7.14 (dd, *J* = 7.6, 8.0 Hz, 1H, H-4), 7.29 (d, *J* = 2.0 Hz, 2H, H-2′, 6′), 7.44 (d, *J* = 8.0Hz, 1H, H-6), 7.70 (d, *J* = 16.0 Hz, 1H, H-α), 7.80 (d, *J* = 15.6Hz, 1H, H-β), 12.70 (s, OH, 1H at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 55.8, 113.6, 115.5, 118.4, 120.8, 128.0, 128.3, 129.3, 129.8, 131.1, 137.1, 137.6, 141.7, 159.9, 161.7, 193.7; **LC-MS (ESI, positive ion mode):** *m/z* 267 $[M - H]^-$.



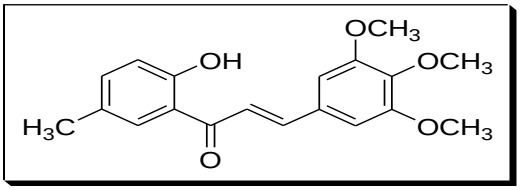
3b

2-Hydroxy-5-methyl-3′, 4′-dimethoxychalcone (3b): Mp: 117-119 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 3.89 (s, 3H, OCH_3 at C-3′), 3.92 (s, 3H, OCH_3 at C-4′), 6.84 (d, *J* = 8.0Hz, 1H, H-3), 6.89 (d, *J* = 8.0 Hz, 1H, H-5′), 7.08 (dd, *J* = 7.6, 8.0Hz, 1H, H-4), 7.11 (d, *J* = 2.0 Hz, 1H, H-2′), 7.22 (dd, *J* = 8.0, 2.0 Hz, 1H, H-6′),7.42 (d, *J* = 7.6 Hz, 1H, H-6), 7.70 (m, 2H, H-α, β), 12.7 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 55.4, 55.7, 103.5, 106.2, 118.6, 119.5, 119.6, 128.2, 129.3, 129.8, 130.9, 137.4, 140.6, 145.7, 153.5, 161.8, 193.8; **LC-MS (ESI, negative ion mode):** *m/z* 297 $[M - H]^-$.



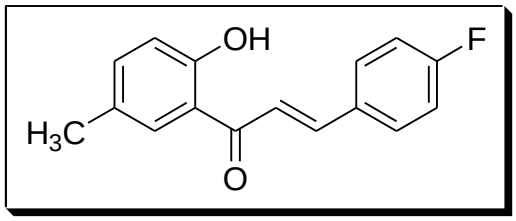
3c

2-Hydroxy-5-methyl -4′-chlorochalcone (3c): Mp: 132-134 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 6.81 (d, *J* = 8.0 Hz, 1H, H-3), 7.11 (dd, *J* = 7.8, 8.0 Hz, 1H, H-4), 7.37 (d, *J* = 8.8 Hz, 2H, H-3′, 5′),7.43 (d, *J* = 7.6 Hz, 1H, H-6), 7.53 (d, *J* = 8.4 Hz, 2H, H-2′, 6′), 7.70 (d, *J* = 15.6 Hz, 1H, H-α), 7.80 (d, *J* = 15.6 Hz, 1H, H-β), 12.7 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 118.5, 127.9, 128.5, 128.9, 129.3, 129.5, 131.0, 134.2, 135.7, 137.6, 140.3, 161.9, 193.7; **LC-MS (ESI, negative ion mode):** *m/z* 271 $[M - H]^-$.



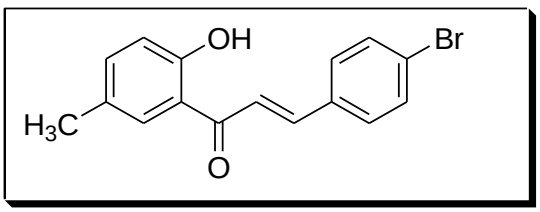
3d

2-Hydroxy-5-methyl-3′, 4′, 5′-trimethoxychalcone (3d): Mp: 116-118 °C; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 3.90 (s, 3H, OCH_3 at C-4′), 4.0 (s, 6H, OCH_3 at C-5′, 3′), 6.84 (d, *J* = 8.0 Hz, 1H, H-3), 7.06 (dd, *J* = 8.0Hz, 1H, H-4), 7.30 (d, *J* =8.8 Hz, 1H, C-2′, 6′), 7.44 (d, *J* = 8.0 Hz, 1H, H-6), 7.75 (d, *J* =15.4 Hz, 1H, H-α), 7.80 (d, *J* = 15.4 Hz, 1H, H- β), 12.7 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ20.7, 56.3, 56.4, 61.1, 103.3, 106.1, 118.5 , 119.5, 119.7, 128.0,129.3, 130.2, 137.6, 140.8, 145.6, 153.6, 161.7, 193.5; **LC-MS (ESI, negative ion mode):** *m/z* 327 [M - H]$^-$.



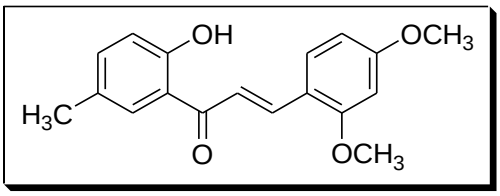
3e

2-Hydroxy-5-methyl-4′-fluorochalcone (3e): Mp: 172-174 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 6.83 (d, *J* = 8.0 Hz, 1H, H-3), 7.13 (dd, *J* = 7.8, 8.0 Hz, 1H, H-4), 7.30 (d, *J* = 8.8 Hz, 2H, H-2′, 6′),7.41 (d, *J* = 7.8 Hz, 1H, H-6), 7.53 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.84 (d, *J* = 16.0 Hz, 1H, H-α), 8.00 (d, *J* = 16.0 Hz, 1H, H-β), 12.8 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 116.3, 118.5, 128.0, 128.3, 129.0, 129.7, 130.5, 131.1, 137.6, 140.4, 160.8, 161.6, 193.1; **LC-MS (ESI, negative ion mode):** *m/z* 255 [M - H]$^-$.



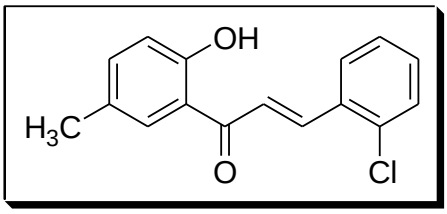
3f

2-Hydroxy-5-methyl-4′-bromochalcone (3f): Mp: 168-170 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 6.85 (d, *J* = 8.0 Hz, 1H, H-3), 7.07 (d, *J* = 7.8, 8.0 Hz, 1H, H-4), 7.43 (d, *J* = 7.8 Hz, 1H, H-6), 7.47 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.50 (d, *J* = 8.4 Hz, 2H, H-2′, 6′), 7.60 (d, *J* = 15.6 Hz, 1H, H-α), 7.85 (d, *J* = 16.0 Hz, 1H, H-β), 12. 7 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6)**: δ 20.7, 118.7, 124.2, 128.0, 128.6, 129.3, 129.6, 130.6, 132.1, 134.6, 137.6, 140.3, 161.8, 193.7; **LC-MS (ESI, negative ion mode):** *m/z* 316 [M - H]$^-$.



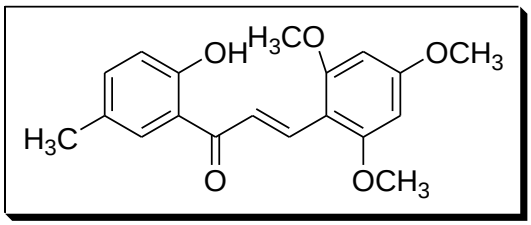
3g

2-Hydroxy-5-methyl-2′,4′-dimethoxychalcone (3g): Mp: 102-104 ^{0}C; **^{1}H-NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 3.84 (s, 3H, OCH_3 at C-4′), 3.93 (s, 3H, OCH_3 at C-2′), 6.40 (d, *J* = 2.2 Hz, 1H, H-3′), 6.52 (dd, *J* = 8.4, 2.2 Hz, 1H, H-5′), 6.83 (d, *J* = 8.0 Hz, 1H, H-3), 7.05 (dd, *J* = 7.6, 8.0Hz, 1H, H-4), 7.45 (d, *J* = 7.6 Hz, 1H, H-6), 7.54 (d, *J* = 8.4 Hz, 1H, H-6′), 7.89 (d, *J* = 15.6 Hz, 1H, H-α), 8.10 (d, *J* = 15.6 Hz, 1H, H-β), 12.09 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 55.3, 55.4, 98.4, 110.6, 117.8, 118.7, 126.8, 128.0, 129.3, 130.2, 130.6, 137.6,139.8, 160.1, 160.9, 161.8,193.9; **LC-MS (ESI, negative ion mode):** *m/z* 297 [M - H]$^-$.



3h

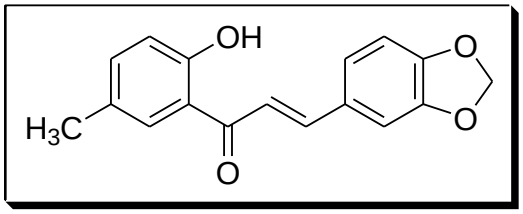
2-Hydroxy-5-methyl -2′-chlorochalcone (3h): Mp: 128-130 ^{0}C; **^{1}H-NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 6.84 (d, *J* = 8.0 Hz, 1H, H-3), 7.14 (dd, *J* = 7.8, 8.0 Hz, 1H, H-4), 7.32 (m, 2H, H-3′, 6′), 7.44 (d, *J* = 7.8 Hz, 1H, H-6), 7.43 (m, 1H, H-5′), 7.69 (m, 1H, H-4′), 7.84 (d, *J* = 16.0 Hz, 1H, H-α), 8.12 (d, *J* = 15.6 Hz, 1H, H-β), 12.79 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** 20.7, 118.7, 126.9, 127.6, 127.8, 128.0, 29.3, 130.2, 130.5, 130.6,134.1, 135.3, 137.6,139.4, 161.8, 193.0; **LC-MS (ESI, negative ion mode):** *m/z* 271 [M - H]$^-$.



3i

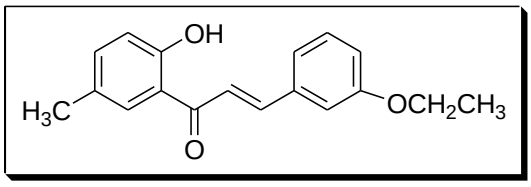
2-Hydroxy-5-methyl-2′,4′,6′-trimethoxychalcone (3i): Mp: 115-117 ^{0}C; **^{1}H-NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 3.90 (s, 6H, OCH_3 at C-2′, 6′), 3.92 (s, 3H, OCH_3 at C-4′), 6.13 (2H, s, H-3′, 5′), 6.81 (d, *J* = 8.0 Hz, 1H,

H-3), 7.09 (dd, *J* = 7.6, 8.0 Hz, 1H, H-4), 7.42(d, *J* = 7.6 Hz, 1H, H-6), 7.90 (d, *J* = 15.6 Hz, H-α), 8.12 (d, *J* = 15.6 Hz, 1H, H-α), 12.8 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 55.3, 55.7, 90.7, 107.3, 118.6, 127.5, 128.6, 129.3, 130.6, 137.6, 139.8, 160.9, 161.6, 161.8, 192.7; **LC-MS (ESI, negative ion mode):** *m/z* 327 [M - H]$^-$.



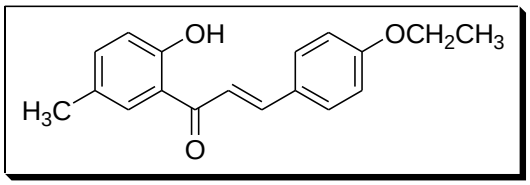
3j

2-Hydroxy-5-methyl-4,6-dimethoxy-[1′,3′]-dioxochalcone (3j): Mp: 190-193 ºC; **^{1}H-NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 6.01 (brs, 2H, H-2′), 6.86 (d, *J* = 8.0Hz, 1H, H-3), 7.02 (dd, *J* = 8.0, 2.0 Hz, 1H, H-6′), 7.10 (d, *J* = 2.0 Hz, 1H, H-8′),7.12 (dd, *J* = 7.8, 8.0 Hz, 1H, H-4), 7.35 (d, *J* = 8.0 Hz, 1H, H-5′), 7.41 (d, *J* = 7.8 Hz, 1H, H-6), 7.71 (brs, 2H, H-α, β), 12.8 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 101.4, 106.6, 108.6, 118.5, 124.8, 126.1, 128.1, 129.4, 130.2, 137.6, 141.9, 148.3, 149.4, 161.8, 192.7; **LC-MS (ESI, negative ion mode):** *m/z* 381 [M - H]$^-$.



3k

2-Hydroxy-5-methyl- 3′-ethoxychalcone (3k): Mp: 101-103 ºC; **^{1}H NMR (DMSO-d_6):** δ 1.37 (t, *J* = 6.8 Hz, 3H, -CH_2-CH_3), δ 2.4 (s, 3H, CH_3 at C-5), 4.11 (q, *J* = 7.2 Hz, 2H, O-CH_2-CH_3), 6.85 (d, *J* = 8.0 Hz, 1H, H-3), 7.01 (dd, *J* = 8.0, 2.2 Hz, 1H, H-4′), 7.07 (dd, *J* = 7.2, 8.0 Hz, 1H, H-4), 7.24 (d, *J* = 2.2 Hz, 1H, H-2′), 7.30 (dd, *J* = 7.2, 2.2 Hz, 1H, H-6′), 7.36 (m, 1H, H-5′),7.44 (d, *J* = 7.2 Hz, 1H, H-6), 7.60 (d, *J* = 16.0 Hz, 1H, H-α), 7.80 (d, *J* = 15.6 Hz, 1H, H-β), 12.80 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 14.5, 20.7, 63.1, 114.1, 116.6, 118.5, 120.4, 127.1, 128.1, 129.4, 130.1, 130.6, 136.3, 137.6, 141.7, 158.9, 161.8, 192.7; **LC-MS (ESI, negative ion mode):** *m/z* 281 [M - H]$^-$.

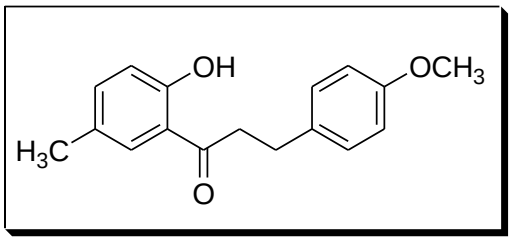


3l

2-Hydroxy-5-methyl-4′-ethoxychalcone (3l): Mp: 92-95 ºC; **^{1}H NMR (DMSO-d_6):** δ 1.37 (t, *J* = 6.8 Hz, 3H, -OCH_2-CH_3), δ 2.3 (s, 3H, CH_3 at C-5), 4.12 (q, *J* = 7.8 Hz, 2H, -OCH_2-CH_3), 6.82 (d, *J* = 8.0Hz, 1H, H-3), 7.06 (dd, *J* = 7.2, 8.0Hz, 1H, H-4), 7.41 (d, *J* = 7.2 Hz, 1H, H-6), 7.62 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.69 (d, *J* = 8.8 Hz, 2H, H-2′, 6′), 7.73 (d, *J* = 15.6 Hz, 1H, H-α), 7.81 (d, *J* = 16.0 Hz, 1H, H-β), 12.70 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 14.5 ,20.7 ,, 63.3,118.5 ,120.4,127.3 ,128.1,129.4 , 130.3, 130.6 ,135.3.3,137.6 ,142.3,158.9,160.4,161.8 ,192.7; **LC-MS (ESI, negative ion mode):** *m/z* 281 [M - H]$^-$.

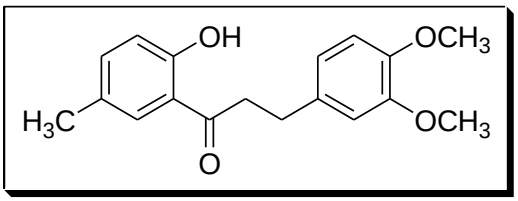
General procedure for the preparation of dihydrochalcones: (4a-4l)

To a solution of chalcone (**4a-4l**) **(**4 mmol) in methanol (80 mL) 10 % Pd-C (1000 mg) was added and the reaction mixture was stirred under hydrogen atmosphere for 2 h at room temperature. After completion of the reaction, the catalyst was filtered off and the reaction mixture was concentrated. The residue obtained after concentration was chromatographed over silica gel column using hexane-EtOAc mixtures as eluent to give pure dihydrochalcone.



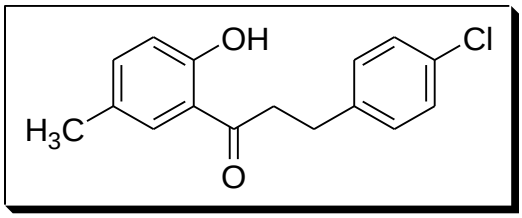
4a

2-Hydroxy-5-methyl-4′-methoxydihydrochalcone (4a): Mp: 125-128 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.84 (t, *J* = 7.2 Hz, 2H, H-β), 3.36 (t, *J* = 7.2 Hz, 2H, H-α), 3.84 (s, 3H, OCH_3 at C-3′), 6.73 (d, *J* = 8.0Hz, 1H, H-3), 7.11 (dd, *J* = 8.0Hz, 1H, H-4), 7.51 (d, *J* = 8.0Hz, 1H, H-6) 6.93 (d, *J* = 8.0 Hz, 2H, H-3′, 5′), 7.27 (d, *J* = 8.0 Hz, 2H, H- 2′, 6′), 12.70 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 26.4, 39.8, 55.8, 113.6, 115.5, 117.4, 120.8, 127.6, 128.6, 129.2, 129.8, 136.5, 137.1, 159.9, 160.2, 201.2; **LC-MS (ESI, negative ion mode):** *m/z* 269 [M - H]$^-$.



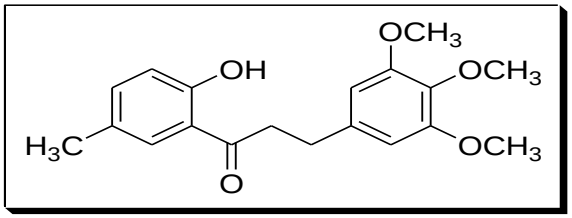
4b

2-Hydroxy-5-methyl-3′,4′-dimethoxydihydrochalcone (4b) Mp: 117-119 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 2.81 (t, 2H, *J* = 7.6 Hz, H-β), 3.86 (t, *J* = 7.6 Hz, 2H, H-α), 3.89 (s, 3H, OCH_3 at C-3′), 3.92 (s, 3H, OCH_3 at C-4′),6.75 (d, *J* = 8.0Hz, 1H, H-3), 7.06 (dd, *J* = 8.0Hz, 1H, H-4), 7.54 (d, *J* = 8.0Hz, 1H, H-6) 6.89 (d, 1H, *J* = 8.0 Hz, H-5′), 7.05 (m, 3H), 7.11 (d, *J* = 2.0 Hz, 1H, H-2′), 7.21 (dd, *J* = 8.0, 2.0 Hz, 1H, H-6′), 12.80 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 29.1, 39.5, 55.4, 55.7, 110.6, 111.3, 117.8, 122.5, 125.9, 127.2, 128.5, 129.5, 136.4, 149.2, 151.1, 160.4, 200.8; **LC-MS (ESI, negative ion mode):** *m/z* 299 [M - H]$^-$.



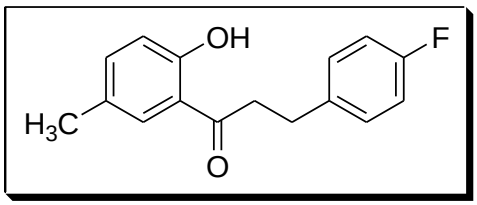
4c

2-Hydroxy-5-methyl-4′-chlorodihydrochalcone (4c): Mp: 162-165 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.84 (t, 2H, *J* = 7.6 Hz, H-β), 3.22 (t, *J* = 7.6 Hz, 2H, H-α), 6.76 (d, *J* = 8.0Hz, 1H, H-3), 7.10 (dd, *J* = 8.0Hz, 1H, H-4), 7.50 (d, *J* = 8.0Hz, 1H, H-6)7.37 (d, *J* = 8.8 Hz, 2H, H-3′, 5′), 7.53 (d, *J* = 8.4 Hz, 2H, H-2′, 6′), 12.71 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 29.0, 40.1, 117.7, 127.5, 128.7, 128.6, 129.4, 129.3, 134.2, 135.7, 136.5, 160.2, 201.9; **LC-MS (ESI, negative ion mode):** *m/z* 273 [M - H]$^-$.



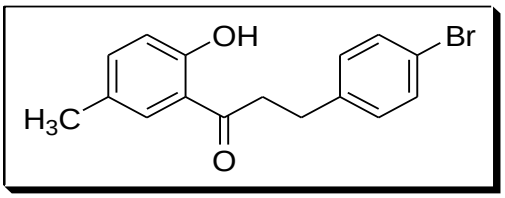
4d

2-Hydroxy-5-methyl-3′,4′,5′-trimethoxydihydrochalcone (4d): Mp: 175-178 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.90 (t, *J* = 7.2 Hz, 2H, H-β), 3.10 (t, *J* = 7.2 Hz, 2H, H-α), 3.92 (s, 6H, OCH_3 at C-5′, 3′), 3.93 (s, 3H, OCH_3 at C-4′), 6.83 (s, 2H, H-2′, 6′), 6.74 (d, *J* = 8.0Hz, 1H, H-3), 7.10 (dd, *J* = 8.0Hz, 1H, H-4), 7.52 (d, *J* = 8.0Hz, 1H, H-6)12.73 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 29.3, 39.4, 55.2, 55.9, 117.3, 127.4, 127.6, 128.4, 129.8, 136.2, 141.9, 153.4, 160.3, 200.6; **LC-MS (ESI, negative ion mode):** *m/z* 329 [M - H]$^-$.



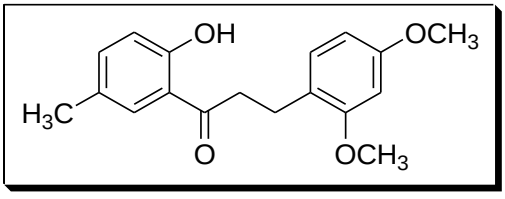
4e

2-Hydroxy-5-methyl-4′-fluorodihydrochalcone (4e): Mp: 141-143 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.74 (t, *J* = 7.8 Hz, 2H, H-β), 3.20 (t, *J* = 7.8 Hz, 2H, H-α), 6.77 (d, *J* = 8.0Hz, 1H, H-3), 7.07 (dd, *J* = 8.0Hz, 1H, H-4), 7.53 (d, *J* = 8.0Hz, 1H, H-6)7.30 (d, *J* = 8.8 Hz, 2H, H-2′, 6′), 7.53 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 12.80 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 29.6, 40.7, 116.3, 117.6, 127.7, 128.8, 129.1, 129.7, 131.1, 136.8, 160.8, 160.5, 202.4; **LC-MS (ESI, negative ion mode):** *m/z* 257 [M - H]$^-$.



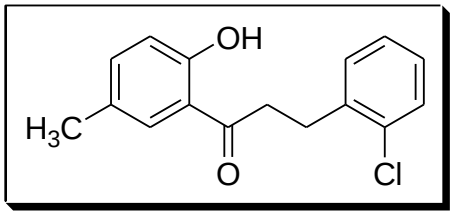
4f

2-Hydroxy-5-methyl-4′-bromodihydrochalcone (4f): Mp: 158-160 ^{0}C; **^{1}H-NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.84 (t, *J* = 7.6 Hz, 2H, H-β), 3.22 (t, *J* = 7.6 Hz, 2H, H-α), 6.76 (d, *J* = 8.0Hz, 1H, H-3), 7.09 (dd, *J* = 8.0Hz, 1H, H-4), 7.50 (d, *J* = 8.0Hz, 1H, H-6)7.44 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.50 (d, *J* = 8.4 Hz, 2H, H-2′, 6′), 12.71 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 29.0, 40.1, 117.2, 124.2, 127.2, 128.4, 128.6, 129.2, 132.1, 134.6, 136.3, 160.6, 203.1; **LC-MS (ESI, negative ion mode):** *m/z* 318 [M - H]$^-$.



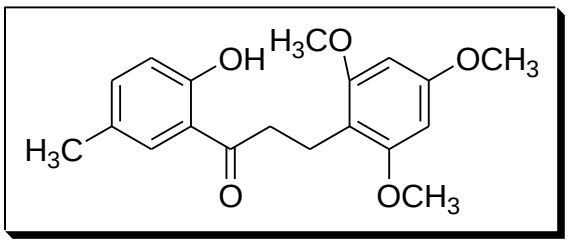
4g

2-Hydroxy-5-methyl-2′, 4′-dimethoxydihydrochalcone (4g): Mp: 172-174 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.88 (t, *J* = 7.2Hz, 2H, H-β), 3.12 (t, *J* = 7.2 Hz, 2H, H-α), 3.85 (s, 3H, OCH_3 at C-4′), 3.84 (s, 3H, OCH_3 at C-2′), 6.40 (d, *J* = 2.2 Hz, 1H, H-3′), 6.52 (dd, *J* = 8.4, 2.2 Hz, 1H, H-5′), 6.72 (d, *J* = 8.0Hz, 1H, H-3), 7.08 (dd, *J* = 8.0Hz, 1H, H-4), 7.49 (d, *J* = 8.0Hz, 1H, H-6)7.54 (d, *J* = 8.4 Hz, 1H, H-6′), 12.72 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 29.3, 39.4, 55.3, 55.4, 98.4, 110.6, 117.4, 127.6, 128.1, 129.4, 130.2, 136.7, 160.9, 202.4; **LC-MS (ESI, negative ion mode):** *m/z* 299 [M - H]$^-$.



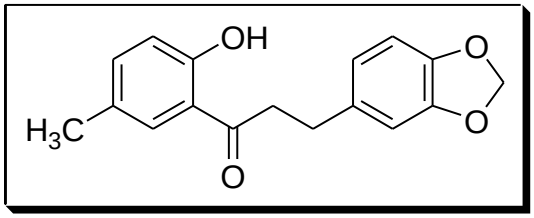
4h

2-Hydroxy-5-methyl-2′-chlorodihydrochalcone (4h): Mp: 165-168 ^{0}C; **^{1}H-NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.84 (t, *J* = 7.2 Hz, 2H, H-β), 3.36 (t, *J* = 7.2 Hz, 2H, H-α), 6.73 (d, *J* = 8.0Hz, 1H, H-3), 7.10 (dd, *J* = 8.0Hz, 1H, H-4), 7.53 (d, *J* = 8.0Hz, 1H, H-6)7.32 (m, 2H, H-3′, 6′), 7.43 (t, *J* = 8.0 Hz, 1H, H-5′), 7.68 (t, *J* = 8.0 Hz, 1H, H-4′), 12.80 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 26.4, 39.8, 117.5, 127.1, 127.6, 127.8, 128.3,129.6, 130.2, 130.5, 134.1, 135.3, 136.4, 160.2, 201.7; **LC-MS (ESI, negative ion mode):** *m/z* 273 [M - H]$^-$.



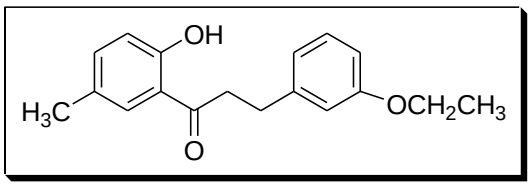
4i

2-Hydroxy-5-methyl -2′,4′,6′-trimethoxydi hydrochalcone (4i): Mp: 162-164 ^{0}C; **^{1}H-NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-5), 2.89 (t, *J* = 7.5 Hz, 2H, H-β), 3.14 (t, *J* = 7.5 Hz, 2H, H-α), 3.90 (s, 6H, OCH_3 at C-2′, 6′), 3.92 (s, 3H, OCH_3 at C-4′), 6.13 (s, 2H, H-3′, 5′), 6.75 (d, *J* = 8.0Hz, 1H, H-3), 7.05 (dd, *J* = 8.0Hz, 1H, H-4), 7.52 (d, *J* = 8.0Hz, 1H, H-6)12.70 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 26.8, 39.0, 55.3, 55.7,90.7, 107.3, 117.8, 127.5, 128.7, 129.8, 136.1, 160.8, 160.9, 161.6, 200.5; **LC-MS (ESI, negative ion mode):** *m/z* 329 [M - H]$^-$.



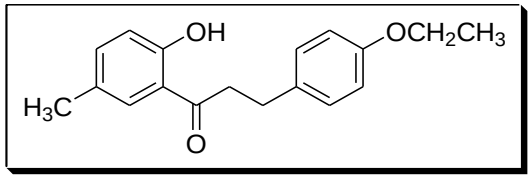
4j

2-Hydroxy-5-methyl-[1′,3′]-dioxodihydrochalcone (4j): Mp: 158-160 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-5), 2.74 (t, *J* = 7.2 Hz, 2H, H-β), 3.16 (t, *J* = 7.2 Hz, 2H, H-α), 6.01 (brs, 2H, H-2′), 7.01 (dd, *J* = 8.0, 2.0 Hz, 1H, H-6′), 6.77 (d, *J* = 8.0Hz, 1H, H-3), 7.06 (dd, *J* = 8.0Hz, 1H, H-4), 7.54 (d, *J* = 8.0Hz, 1H, H-6)7.08 (d, *J* = 2.0 Hz, 1H, H-8′), 7.34 (d, *J* = 8.0 Hz, 1H, H-5′), 12.75 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.2, 40.9, 101.4, 106.6, 108.6, 117.2, 124.8, 127.8, 128.4, 129.3, 130.2, 136.6, 148.3, 149.4, 160.1, 203.5; **LC-MS (ESI, negative ion mode):** *m/z* 283 [M - H]$^-$.



4k

2-Hydroxy-5-methyl-3′-ethoxydihydrochalcone (4k): Mp: 99-102 ^{o}C; **^{1}H NMR (DMSO-d_6):** δ 1.37 (t, *J* = 6.8 Hz, 3H, -CH_2-CH_3), 2.3 (s, 3H, CH_3 at C-5), 2.74 (t, *J* = 7.2 Hz, 2H, H-β), 3.16 (t, *J* = 7.2 Hz, 2H, H-α), 4.11 (q, *J* = 7.2 Hz, 2H, O-CH_2-CH_3), 7.01 (dd, *J* = 7.6, 2.2 Hz, 1H, H-4′), 6.74 (d, *J* = 8.0Hz, 1H, H-3), 7.10 (dd, *J* = 8.0Hz, 1H, H-4), 7.51 (d, *J* = 8.0Hz, 1H, H-6)7.24 (d, *J* = 2.2 Hz, 1H, H-2′), 7.30 (dd, *J* = 7.2, 2.2 Hz, 1H, H-6′), 7.36 (m, 1H, H-5′), 12.70 (s, 1H, OH at C-2); **^{13}CNMR (DMSO-d_6):** δ 14.5, 20.7, 29.3, 39.8 ,63.1, 114.1, 116.6, 117.3, 120.4, 127.3, 128.2, 129.8, 130.1, 136.3, 136.5, 158.9, 160.4, 202.1; **LC-MS (ESI, negative ion mode):** *m/z* 283 [M - H]$^-$.

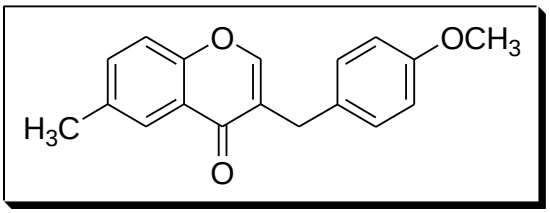


4l

2-Hydroxy-5-methyl-4′-ethoxydihydrochalcone (4l): Mp: 86-88 ºC; **^{1}H NMR (DMSO-d_6):** δ 1.37 (t, *J* = 6.8 Hz, 3H, -OCH_2-CH_3), 2.4 (s, 3H, CH_3 at C-5), 2.84 (t, *J*=7.6 Hz, 2H, H-β), 3.22 (t, *J* = 7.6 Hz, 2H, H-α), 4.12 (q, *J* = 7.8 Hz, 2H, -OCH_2-CH_3), 6.72 (d, *J* = 8.0Hz, 1H, H-3), 7.07(dd, *J* = 8.0Hz, 1H, H-4), 7.49 (d, *J* = 8.0Hz, 1H, H-6) 7.62 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.69 (d, *J* = 8.8 Hz, 2H, H-2′, 6′), 12.70 (s, 1H, OH at C-2); **^{13}C NMR (DMSO-d_6):** δ 14.5, 20.7, 26.8, 39.8, 63.3, 117.5, 120.4, 127.1, 128.3, 129.7, 130.3, 135.3, 136.7, 160.5, 202.9; **LC-MS (ESI, negative ion mode):** *m/z* 283 $[M - H]^-$.

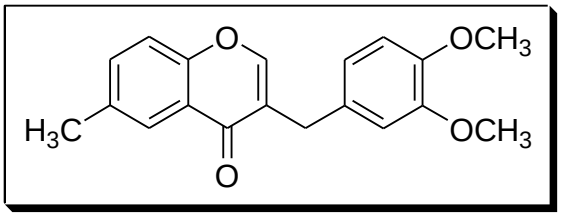
General procedure for the preparation of 6-*C*-methylated homoisoflavones (5a-5l)

A mixture of dihydrochalcones **(4)** (3 mmol) and $BF_3.Et_2O$ (1.2 mL, 9 mmol) was cooled to 10 ^{0}C and DMF (4.6 mL) was added drop wise for 5 min. In another flask, DMF (8 mL) was cooled to 10 ^{0}C and PCl_5 (0.939 g, 4.5 mmol) was added in small portions. The mixture was then allowed to stand to 55 ^{0}C for 20 min. the light yellow colored solution containing N,N′-dimethyl(chloromethylene) ammonium chloride was then added to the above reaction mixture slowly at 20-25 ^{0}C. The reaction mixture was stirred at room temperature for 2 h and poured into boiling dil. HCl slowly and cooled. The solution was extracted with water (20 mL), brine (20 mL) and dried over sodium sulfate. The residue obtained after evaporation of the solvent was chromatographed over silica gel column using hexane-ethyl acetate mixtures as eluent to give 6-*C*-methylated homoisoflavones.



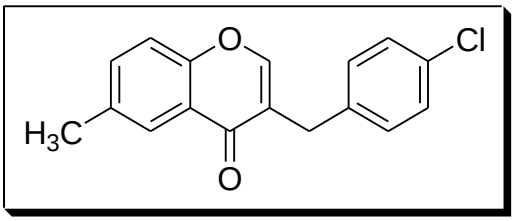
5a

3-(4′-Methoxybenzyl)--6-methyl-4*H*-chromen-4-one (5a): Mp: 175-180 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-6), 3.50 (s, 2H, H-9), 3.81 (s, 3H, OCH_3 at C-4′), 6.83 (d, *J* = 8.8 Hz, 1H, H-8), 6.98 (d, *J* = 8.0Hz, 2H, H-3′, 5′), 7.09 (dd, *J* = 3.2, 8.8 Hz, 1H, H-7), 7.26 (d, *J* = 8.0 Hz, 2H, H-2′, 6′), 7.44 (d, *J* = 3.2 Hz, 1H, H-5), 7.89 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.8, 55.8, 103.8, 108.1, 114.3, 115.1, 121.5, 128.9, 130.1, 132.2, 135.60, 152.0, 160.38, 162.47, 176.0; **LC-MS (ESI, positive ion mode):** *m/z* 281 $[M+H]^+$; Anal. calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.123; H, 5.753.



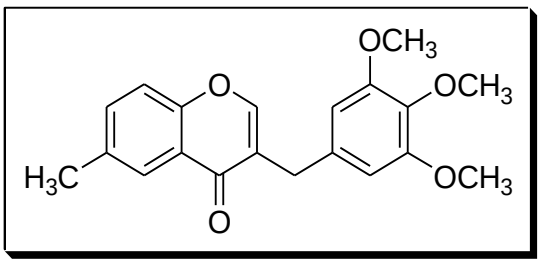
5b

3-(3′,4′-Dimethoxybenzyl)-6-methyl-4*H*-chromen-4-one (5b): Mp: 190-195 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-6), 3.56 (s, 2H, H-9), 3.89 (s, 3H, OCH_3 at C-3′), 3.92 (s, 3H, OCH_3 at C-4′), 6.89 (d, *J* = 8.0 Hz, 1H, H-5′), 6.91 (d, *J* = 8.8 Hz, 1H, H-8), 7.10 (dd, *J* = 3.2 Hz, 1H, H-7), 7.11 (d, *J* = 2.0 Hz, 1H, H-2′), 7.21 (dd, *J* = 8.0, 2.0 Hz, 1H, H-6′), 7.42 (d, J=3.2 Hz, 1H, H-5), 8.14 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** 20.7, 30.7, 55.4, 55.7, 110.6, 111.3, 114.9, 118.1, 121.8, 122.5, 125.9, 129.9, 131.4, 137.2, 149.2, 149.7, 151.3, 151.1, 176.3; **LC-MS (ESI, positive ion mode):** *m/z* 311 $[M + H]^+$; Anal. calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.53; H, 5.84.



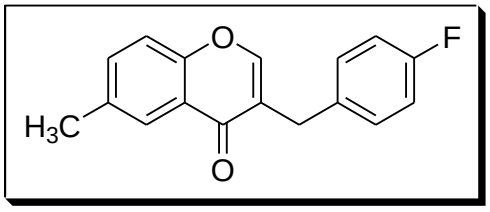
5c

3-(4′-Chlorobenzyl)-6-methyl-4*H*-chromen-4-one (5c): Mp: 210-214 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-6), 3.46 (s, 2H, H-9), 6.92 (d, 1H, *J* = 8.8 Hz, H-8), 7.11 (dd, 1H, *J* = 3.2, 8.8 Hz, H-7), 7.37 (d, 2H, *J* = 8.8 Hz, H-3′, 5′), 7.43 (d, J=3.2 Hz, 1H, H-5), 7.53 (d, *J* = 8.4 Hz, 2H, H-2′, 6′), 7.95(s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.6, 114.9, 118.1, 121.5, 128.5, 129.3, 129.9, 131.4, 134.2, 135.7, 137.2, 149.7, 151.5, 176.5; **LC-MS (ESI, positive ion mode):** *m/z* 285 $[M + H]^+$; Anal. calcd. for $C_{17}H_{13}O_2Cl$: C, 71.71; H, 4.60. Found: C, 71.70; H, 4.601.



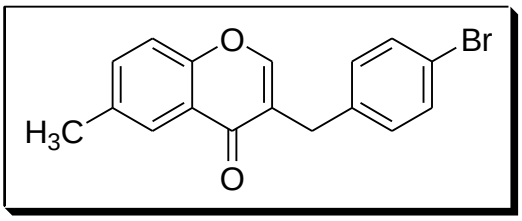
5d

3-(3′,4′,5′-Trimethoxybenzyl)-6-methyl-4*H*-chromen-4-one (5d): Mp: 250-253 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-6), 3.61 (s, 2H, H-9), 3.92 (s, 6H, OCH_3 at C-5′, 3′), 3.93 (s, 3H, OCH_3 at C-4′), 6.83 (s, 2H, H-2′, 6′),6.92 (d, *J* = 8.8 Hz, 1H, H-8), 7.10 (dd, *J* = 2.9, 8.8 Hz, 1H, H-7), 7.44 (d, J=3.2 Hz, 1H, H-5), 8.21 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.5, 55.2, 55.9, 114.9, 118.1, 121.9, 127.3, 129.9, 131.4, 137.2, 141.9, 149.7, 151.7, 153.4, 175.9; **LC-MS (ESI, positive ion mode):** *m/z* 341 $[M + H]^+$; Anal. calcd. for $C_{22}H_{24}O_7$: C, 70.57; H, 5.92. Found: C, 70.574; H, 5.93.



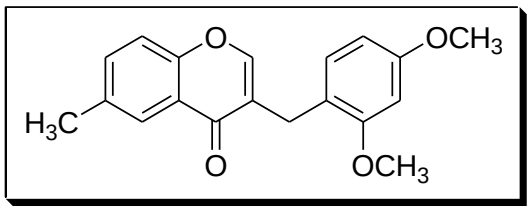
5e

3-(4′-Fluorobenzyl)-6-methyl-4*H*-chromen-4-one (5e): Mp: 185-190 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-6), 3.52 (s, 2H, H-9), 6.92 (d, *J* = 8.9 Hz, 1H, H-8), 7.11 (dd, *J* = 3.0, 8.9 Hz, 1H, H-7), 7.30 (d, *J* = 8.8 Hz, 2H, H-2′, 6′), 7.46 (d, J=3.2 Hz, 1H, H-5), 7.53 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 8.09 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.8, 114.9, 116.3, 118.1, 121.7, 129.7, 129.9, 131.1, 131.4, 137.2, 149.7, 151.9, 175.8; **LC-MS (ESI, positive ion mode):** *m/z* 269 $[M + H]^+$; Anal. calcd. for $C_{17}H_{13}O_2F$: C, 76.11; H, 4.88. Found : C, 76.10; H, 4.884.



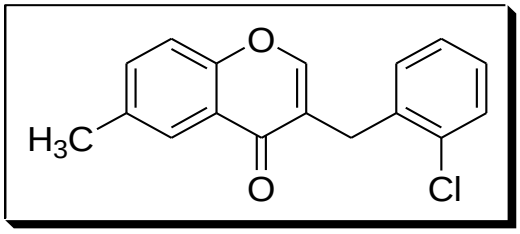
5f

3-(4′-Bromobenzyl)-6-methyl-4*H*-chromen-4-one (5f): Mp: 195-200 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.4 (s, 3H, CH_3 at C-6), 3.49 (s, 2H, H-9), 6.90 (d, *J* = 8.8 Hz, 1H, H-8), 7.09 (dd, *J* = 3.2, 8.8 Hz, 1H, H-7), 7.45 (d, J=3.2 Hz, 1H, H-5), 7.48 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.50 (d, *J* = 8.4 Hz, 2H, H-2′, 6′), 8.03 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.6, 114.9, 118.1, 121.5, 124.2, 128.6, 129.9, 131.4, 132.1, 137.2, 138.4, 149.7, 151.3, 176.2; **LC-MS (ESI, positive ion mode):** *m/z* 330 $[M + H]^+$; Anal. calcd. for $C_{17}H_{13}O_2Br$: C, 62.03; H, 3.98. Found : C, 62.025; H, 3.99.



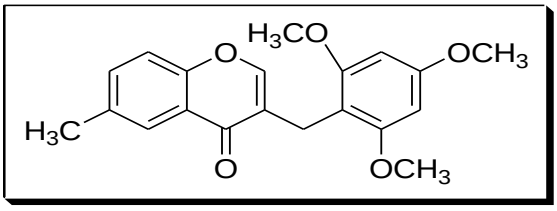
5g

3-(2′,4′-Dimethoxybenzyl)-6-methyl-4*H*-chromen-4-one (5g): Mp: 210-214 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-6), 3.85 (s, 3H, OCH_3 at C-4′), 3.51 (s, 2H, H-9), 3.84 (s, 3H, OCH_3 at C-2′), 6.40 (d, *J* = 2.0 Hz, 1H, H-3′), 6.52 (dd, *J* = 8.4, 2.0 Hz, 1H, H-5′), 6.92 (d, *J* = 8.7 Hz, 1H, H-8), 7.10 (dd, *J* = 3.3, 8.7 Hz, 1H, H-7), 7.40 (d, J=3.3 Hz, 1H, H-5), 7.54 (d, *J* = 8.4 Hz, 1H, H-6′), 7.98 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.7, 55.3, 55.4, 98.4, 110.6, 114.9, 117.8, 118.1, 121.9, 129.9, 130.2, 131.4, 137.2, 149.7, 151.2, 160.1, 160.9, 176.4; **LC-MS (ESI, positive ion mode):** *m/z* 311 $[M + H]^+$; Anal. calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found : C, 73.53; H, 5.84.



5h

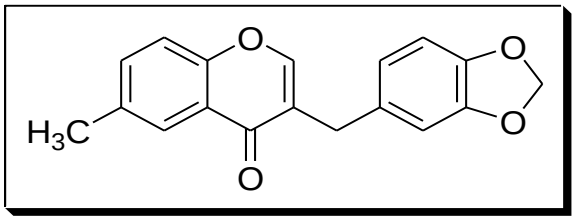
3-(2′-Chlorobenzyl)-6-methyl-4*H*-chromen-4-one (5h): Mp: 195-200 ^{0}C; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-6), 3.53 (s, 2H, H-9), 6.91 (d, *J* = 8.9 Hz, 1H, H-8), 7.12 (dd, *J* = 3.0, 8.9 Hz, 1H, H-7), 7.32 (m, 2H, H-3′, 6′), 7.43 (m, 1H, H-5′), 7.42 (d, J=3.0 Hz, 1H, H-5), 7.68 (m, 1H, H-4′), 7.98 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 20.7, 30.5, 114.9, 118.1, 121.7, 127.6, 127.8, 129.9, 130.2, 130.5, 131.4, 134.1, 135.3, 137.2, 149.7, 152.2, 176.5; **LC-MS (ESI, positive ion mode):** *m/z* 285 $[M + H]^+$; Anal. calcd. for $C_{17}H_{13}O_2Cl$: C, 71.71; H, 4.60. Found: C, 71.70; H, 4.61.



5i

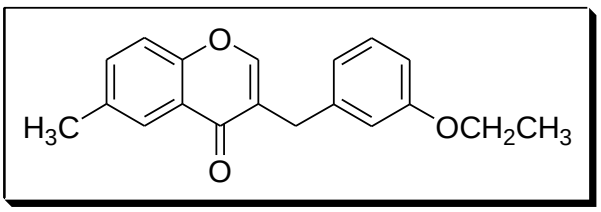
3-(2′,4′,6′-Trimethoxybenzyl)-6-methyl-4*H*-chromen-4-one (5j): Mp: 226-230 ºC; **^{1}H NMR**

(DMSO-d_6): δ 2.3 (s, 3H, CH_3 at C-6), 3.45 (s, 2H, H-9), 3.90 (s, 6H, OCH_3 at C-2′, 6′), 3.92 (s, 3H, OCH_3 at C-4′), 6.13 (s, 2H, H-3′, 5′), 6.91 (d, *J* = 8.9 Hz, 1H, H-8), 7.13 (dd, *J* = 3.0, 8.9 Hz, 1H, H-7), 7.44 (d, J=3.0 Hz, 1H, H-5), 7.98 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** 20.7, 30.8, 55.3, 55.7, 90.7, 107.3, 114.9, 118.1, 121.6, 129.9, 131.4, 137.2, 149.7, 151.8, 160.9, 161.6, 176.3; **LC-MS (ESI, positive ion mode):** *m/z* 341 $[M + H]^+$; Anal. calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.574; H, 5.92.



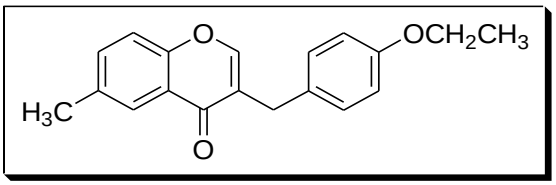
5j

3-((Benzo [*d*] [1,3] dioxol-6-yl) methyl)-6-methyl-4*H*-chromen-4-one (5j): Mp: 210-212 ºC; **^{1}H NMR (DMSO-d_6):** δ 2.3 (s, 3H, CH_3 at C-6), 3.50 (s, 2H, H-9), 6.01 (brs, 2H, H-2′), 6.94 (d, *J* = 9.0 Hz, 1H, H-8),7.02 (d, *J* = 8.0, 2.0 Hz, 1H, H-6′), 7.10 (d, *J* = 2.0 Hz, 1H, H-8′), 7.14 (dd, *J* = 2.9, 9.0 Hz, 1H, H-7), 7.35 (d, *J* = 8.0 Hz, 1H, H-5′), 7.43 (d, J=3.2 Hz, 1H, H-5), 8.10 (s, 1H, H-2); **^{13}C NMR (DMSO-d$_6$):** δ 20.7, 30.6, 101.4, 106.6, 108.6, 114.9, 118.1, 121.8, 124.8, 129.9, 130.2, 131.4, 137.2, 148.3, 149.4, 149.7, 152.1, 176.6; **LC-MS (ESI, positive ion mode):** *m/z* 295 $[M + H]^+$; Anal. calcd. for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.459; H, 4.794.



5k

3-(3′-Ethoxybenzyl)-6-methyl-4*H*-chromen-4-one (5k): Mp: 140-145 ºC; **^{1}H-NMR (DMSO-d_6):** δ 1.37 (t, *J* = 6.8 Hz, 3H, -CH_2-CH_3), 2.3 (s, 3H, CH_3 at C-6), 3.54 (s, 2H, H-9), 4.11 (q, *J* = 7.2 Hz, 2H, O-CH_2-CH_3), 6.92 (d, *J* = 8.8 Hz, 1H, H-8), 7.01 (dd, *J* = 7.6, 2.0 Hz, 1H, H-4′), 7.10 (dd, *J* = 2.9, 8.8 Hz, 1H, H-7), 7.24 (d, *J* = 2.0 Hz, 1H, H-2′), 7.30 (d, *J* = 7.2 Hz, 1H, H-6′), 7.36 (m, 1H, H-5′), 7.45 (d, J=2.9 Hz, 1H, H-5), 7.98 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 14.5, 20.7, 30.5, 63.1, 114.1, 114.9, 116.6, 118.1, 120.4, 121.9, 129.9, 130.1, 131.4, 136.3, 137.2, 149.7, 151.5, 158.9, 176.0; **LC-MS (ESI, positive ion mode):** *m/z* 295 $[M + H]^+$; Anal. calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16 . Found: C, 77.58; H, 6.168.



5l

3-(4′-Ethoxybenzyl)-6-methyl-4*H*-chromen-4-one (5l): Mp: 145-150 ºC; **^{1}H-NMR (DMSO-d_6):** δ 1.37 (t, *J* = 6.8 Hz, 3H, -OCH_2-CH_3), 2.3 (s, 3H, CH_3 at C-6), 3.48 (s, 2H, H-9), 4.12 (q, *J* = 7.8 Hz, 2H, -OCH_2-CH_3), 6.91 (d, *J* = 8.9 Hz, 1H, H-8), 7.12 (dd, *J* = 3.0, 8.9 Hz, 1H, H-7), 7.46 (d, J=3.0 Hz, 1H, H-5), 7.62 (d, *J* = 8.4 Hz, 2H, H-3′, 5′), 7.69 (d, *J* = 8.8 Hz, 2H, H-2′, 6′), 8.05 (s, 1H, H-2); **^{13}C NMR (DMSO-d_6):** δ 14.5, 20.7, 30.7, 63.3, 114.9, 118.1, 120.4, 121.6, 129.9, 130.3, 131.4, 135.3, 137.2, 149.7, 151.4, 160.4, 176.3; **LC-MS (ESI, positive ion mode):** *m/z* 295 $[M + H]^+$; Anal. calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.58; H, 6.168.

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