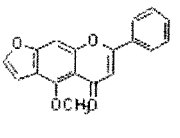
Chapter 3: Section A

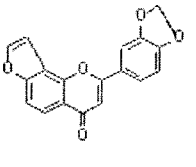
SYNTHESIS OF FUROFLAVONES

3.A.1 Introduction

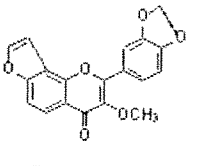
2-Phenyl chromones are a group of flavonoids widely occurring in plants where they play several biological functions.[1] Several naturally occurring flavone derivatives like Pongachalcone I, Quarcetin, Acacetin, Apigenin, Kaempferol, Kanjone and Pongaglaborrone are known to exhibit variety of pharmacological activities.[2-5] Quercetin and related flavonoids are known to inhibit the growth of tumor cells. Flavone-8-acetic acid inhibits endothelial cell proliferation *in-vitro* and selectively destroys tumor vasculature, leading to tumor cell death by ischemia. Flavonoids have also been used as modulators of P-glycoprotein in tumor cells.



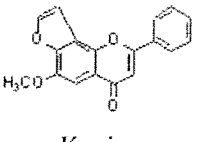
Gamatin



Pongaglabrone



Pongapin



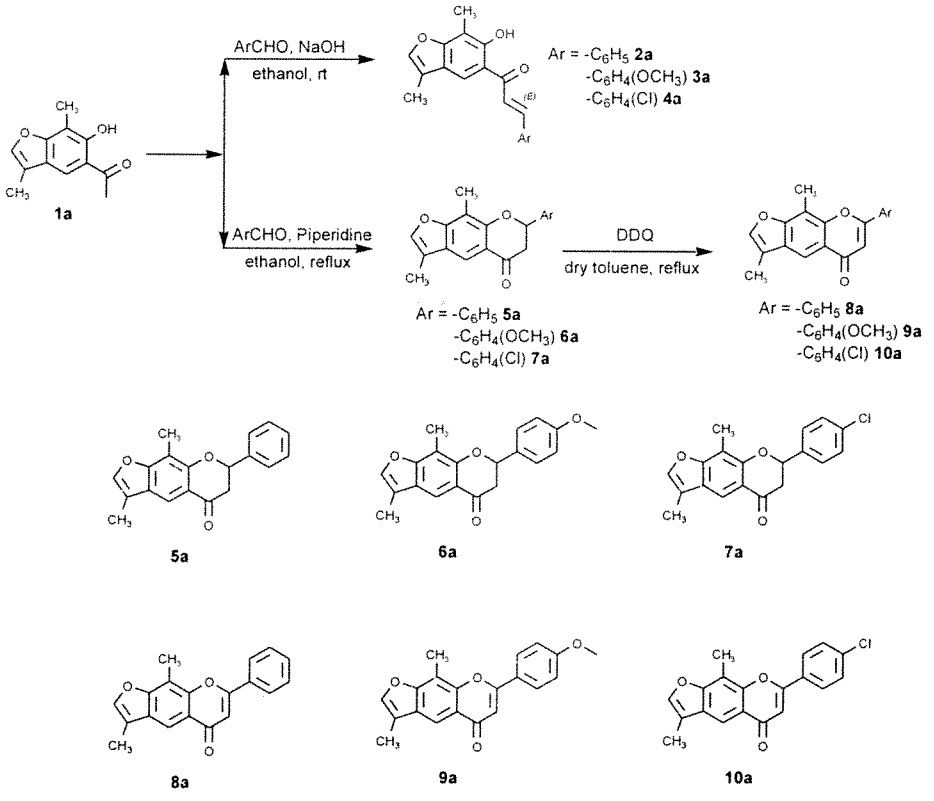
Kanjone

Several methods have been reported for the synthesis of flavonoids in literature.[6,7] Most of the study done hitherto shows the formation of chalcones and flavanones (or flavones) from *ortho*-hydroxy acetophenone in acidic or alkaline conditions.[8] The disadvantage with the basic conditions is the decomposition or retroaldol reaction,[9] whereas acid catalyzed condensation are known to give mixture of chalcone, flavanones & 3-benzylidene flavanones (flavindogenides).[10] Several furoflavanones and furochalcones have been reported to possess interesting pharmacological properties which prompted us to synthesize some new furoflavanones,[11] and study their cytotoxicity behaviour, which has not been reported till date. It was also of considerable interest to study the orientation and conformation of flavanone ring in furoflavanones. Moreover, the α, β-enone

function is a favorable unit for dipolar cycloaddition reaction. This continues our interest in flavonoid chemistry.

Herein, a facile one-pot method of synthesis of some new furoflavanones has been reported. Some of the furoflavones have been screened for *in-vitro* cytotoxicity against human cancer cell lines. The reaction sequence for different title compounds is outlined in **Scheme 1**, **2** and **3**.

3.A.2 Results and Discussion



Scheme 1

1-(6-hydroxy-3,7-dimethylbenzofuran-5-yl)-ethanone **1a**,[12] when condensed with different arylaldehydes in 1% ethanolic sodium hydroxide gave corresponding chalcones (**2a-4a**). Though such a low concentration of alkali was used there was no evidence of formation of flavanones, which was contradictory to the reports in literature which indicated that low concentration of alkali favoured ring closure whereas high concentration of alkali favoured ring fission.[13] ^{1}H NMR of chalcone

E-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone **3a** in $CDCl_3$ **(Figure 1)** exhibited two doublets corresponding to one proton each at δ 7.63-7.67 ppm with *J* 15.6 Hz and δ 7.92-7.96 ppm with *J* 15.6 Hz for C(α)H and C(β)H respectively showing the formation of chalcone in *E* configuration. The broad and shallow IR absorption at 3441 cm^{-1} (*s*) for phenolic –OH indicates strong intramolcular hydrogen bonding. The carbonyl absorption at 1631 cm^{-1}(*s*) along with absorption at 1560 cm^{-1} indicated presence of α, β-unsaturated carbonyl system, which further supports the *E* configuration of chalcone. The furan ring (-C=C-) stretching was observed at 1601cm^{-1}(*s*). The UV spectrum in ethanol showed absorption at 323, 247 and 225 nm.

The mass spectrum (LCMS) of compound *E*-3-(4-chloro-phenyl)-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-propenone **4a** obtained using mobile phase Acetonitrile: Ammonium acetate 1mM (90:10 % v/v) is shown in **Figure 2** which further confirmed the formation of chalcone.

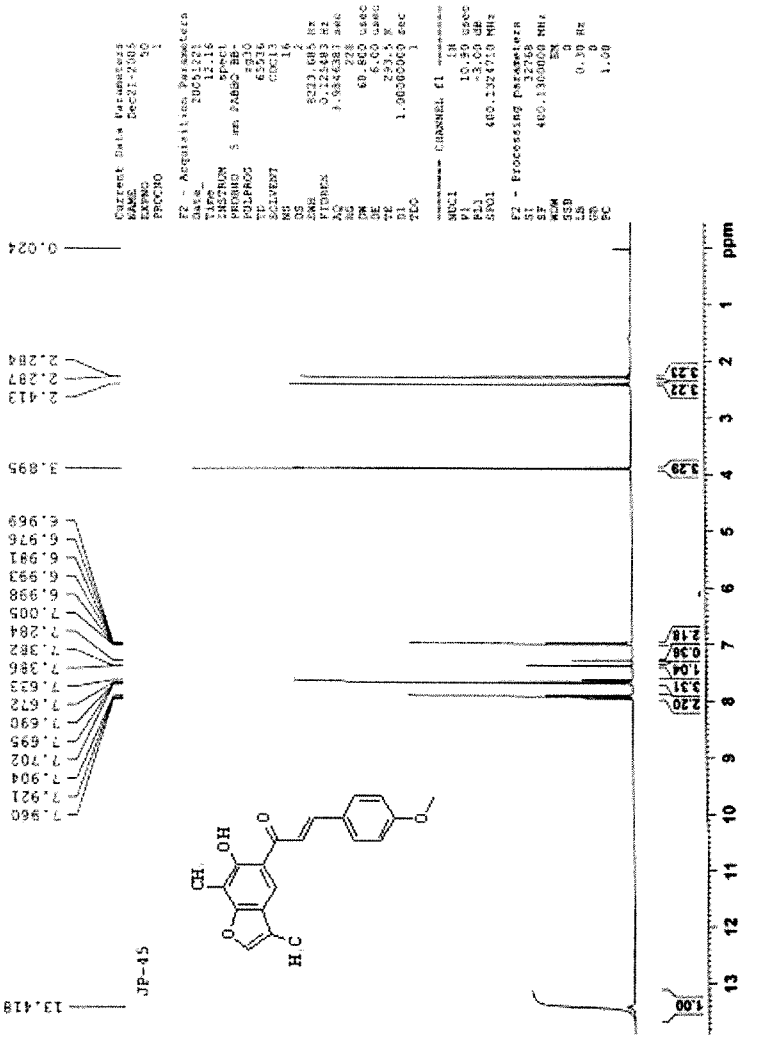


Figure 1: ^{1}H NMR of *E*-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone **3a**. Contd.

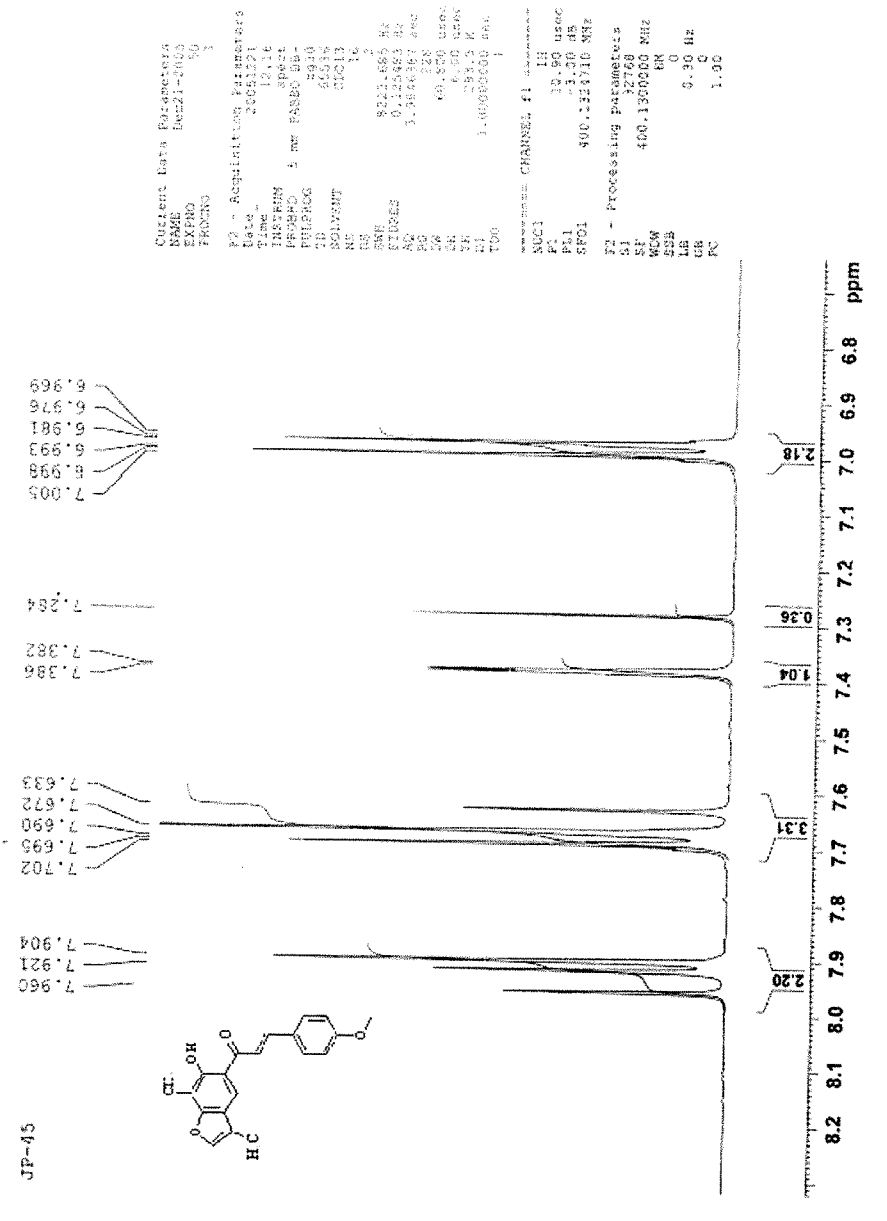


Figure 1: ^{1}H NMR of *E*-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone **3a**.

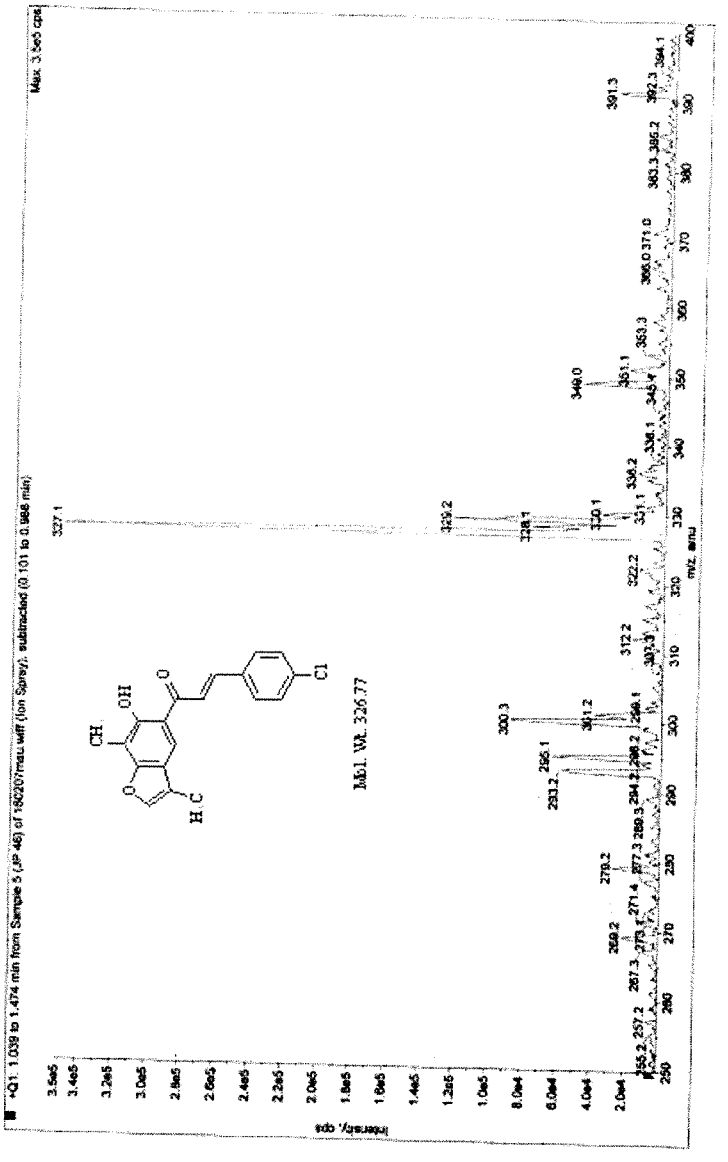


Figure 2: LCMS of *E*-3-(4-chloro-phenyl)-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-propenone **4a**.

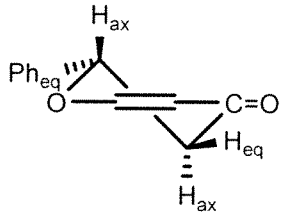


Figure 3: Quasi chair conformation of the flavanone ring.

However, when compound 1-(6-hydroxy-3,7-dimethylbenzofuran-5-yl)-ethanone **1a** was condensed with different aryl aldehydes in presence of catalytic amount of piperidine, it gave a mixture of chalcones and flavanones (**5a-7a**) (**Scheme 1**), flavanone being the major product. The chalcone formation was confirmed by comparison with the isolated chalcones **(2a, 3a, 4a)** on TLC. The flavanone ring exists in quasi chair conformation as shown in **Figure 3**. In the ^{1}H NMR of compound 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **7a** (**Figure 4**), the flavanone ring proton C(2)H appeared as a doublet of doublets at δ 5.48-5.52 ppm. The double doublet for one proton at δ 3.02-3.10 ppm with *J* 16.8 Hz (geminal coupling – diastereotopic protons) and *J* 12.4 Hz (vicinal diaxial coupling) indicated C(3)H proton to be axial and a doublet of doublet at δ 2.89-2.94 ppm with *J* 3.2 Hz (vicinal coupling) and *J*16.8 Hz (geminal coupling – diastereotopic protons) indicated the another proton at C(3) to be equatorial forming an ABX system. The coupling constant of C(2)H proton, 12.4 Hz (vicinal diaxial coupling) and 3.2 Hz (vicinal axial-equatorial coupling) indicated it to be axial in the quasi chair conformation of the flavanone ring, with phenyl ring equatorinal.[14] The ^{13}C NMR **(Figure 5)** of the same compound in $CDCl_3$ with signals at δ 44.61 (C-3 methylene), 77.76 (C-2 oxymethine) and 192.29 (C-4 >C=O) further confirmed the structure of flavanone. The IR **(Figure 6)** absorption at 1683.18 cm^{-1}(*s*) indicated conjugation and hence coplanarity of the carbonyl group with the phenyl ring. The band at 1629cm^{-1}(*s*) indicated (-

C=C-) stretching vibration of the furan ring. The UV spectrum in ethanol showed absorption at 340, 242.60, 227nm. The quasi chair conformation of the flavanone ring is further confirmed by single crystal X-ray diffraction data of **7a** which has been discussed in Section B.

The mass spectrum (LCMS) of compound 7-(4-methoxy-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **6a** obtained using mobile phase Acetonitrile: Ammonium acetate 1mM (90:10 % v/v) is shown in **Figure 7** which further confirmed the formation of flavanone. The base peak at 323.3 indicated M+1 peak.

Figure 4: ^{1}H NMR of compound 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **7a.**

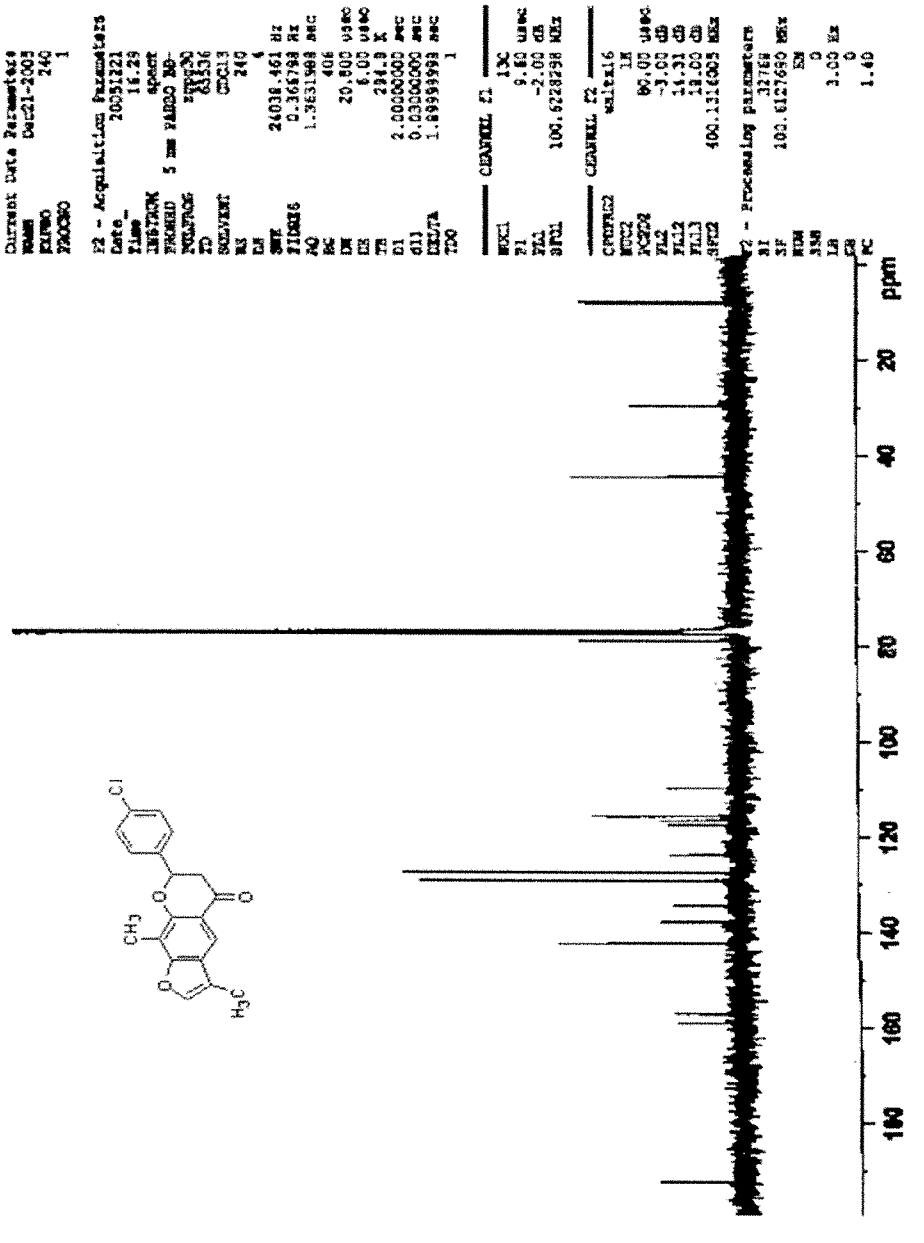


Figure 5: ^{13}C NMR of compound 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **7a.**

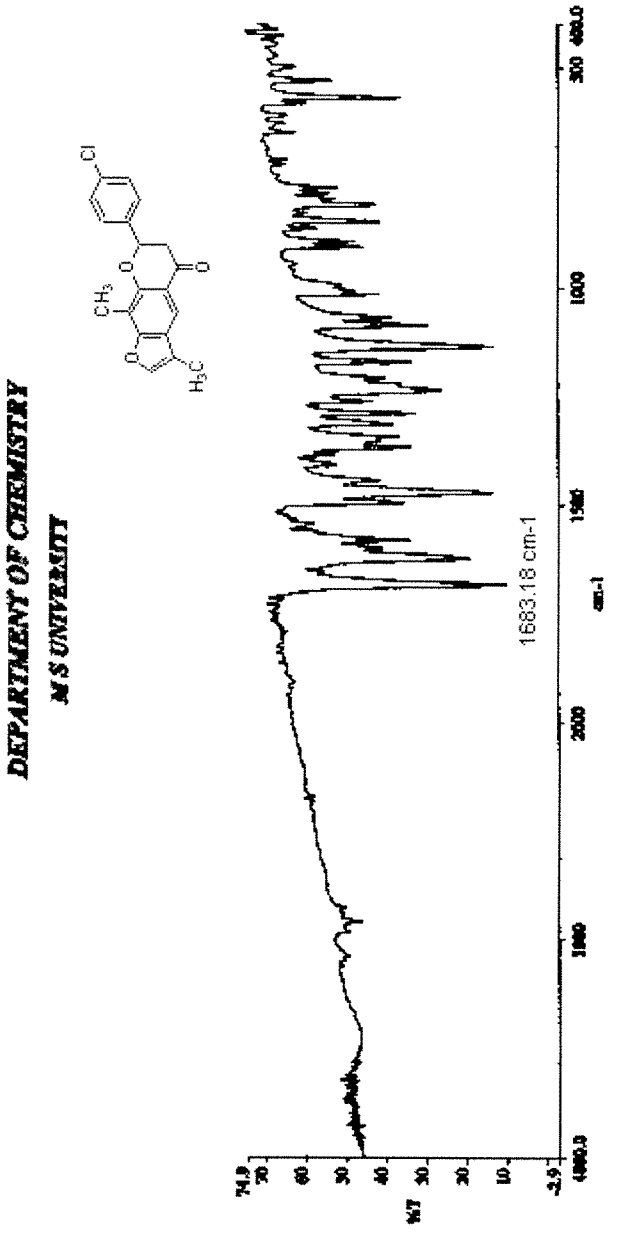


Figure 6: IR of compound 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-g]chromen-5-one **7a.**

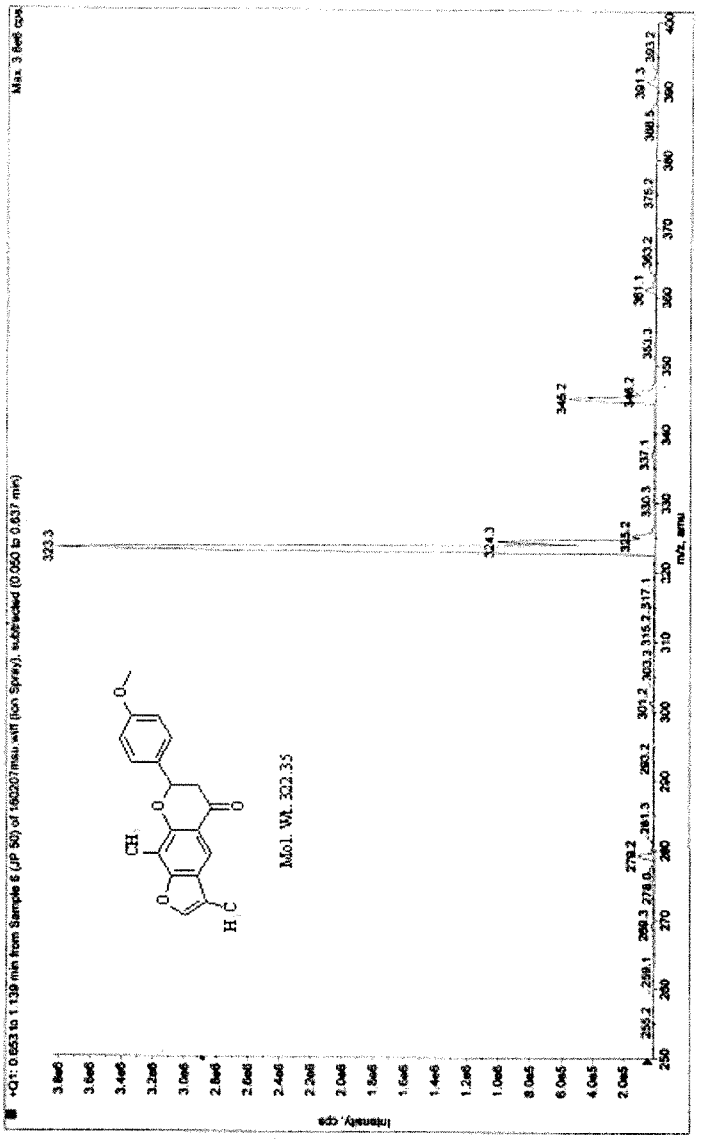
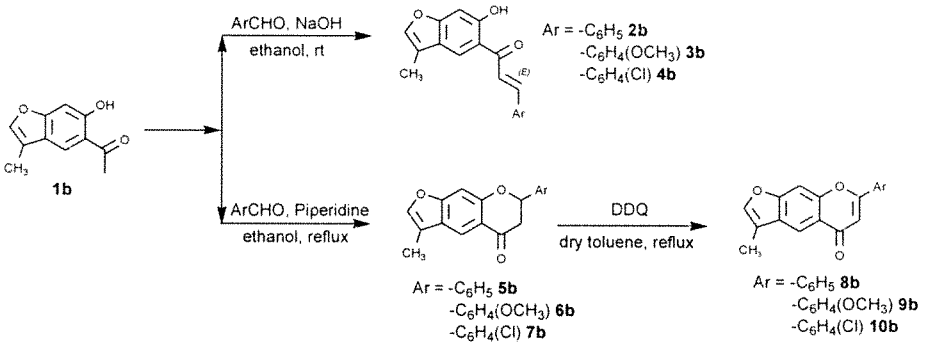


Figure 7: LCMS of 7-(4-methoxy-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **6a**.

Finally, all the flavanones **(5a-7a)** were dehydrogenated to flavones **(8a-10a)** using DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) in dry toluene. In the ^{1}H NMR of compound 7-(4-methoxy-phenyl)-3,9-dimethyl-furo[3,2-*g*]chromen-5-one **9a** in $CDCl_3$ **(Figure 8)**, singlet at δ 6.82 ppm for one proton corresponding to C(3)H of the flavone ring confirms that dehydrogenation has taken place (disappearance of all double doublets). The ^{13}C NMR spectrum **(Figure 9)** of this compound in $CDCl_3$ showed values at δ 104.49 ppm (C-3) and 163.32 ppm (C-2), which supports the dehydrogenated product. In the IR spectrum of this compound, the carbonyl absorption was further lowered and observed at 1651 cm^{-1}(*s*), while (-C=C-) stretching vibration of flavone and furan ring was observed at 1610cm^{-1}(*s*) and 1621 cm^{-1}(*s*) respectively. The UV spectrum in ethanol showed absorption at 307, 278, 245 and 227 nm.



Scheme 2

Similar observations were recorded for the preparation of flavones form 1-(6-hydroxy-3-methyl-benzofuran-5-yl)-ethanone **1b**,[12] **(Scheme2)** as confirmed by spectral data **(Figure 10 – 14)**.

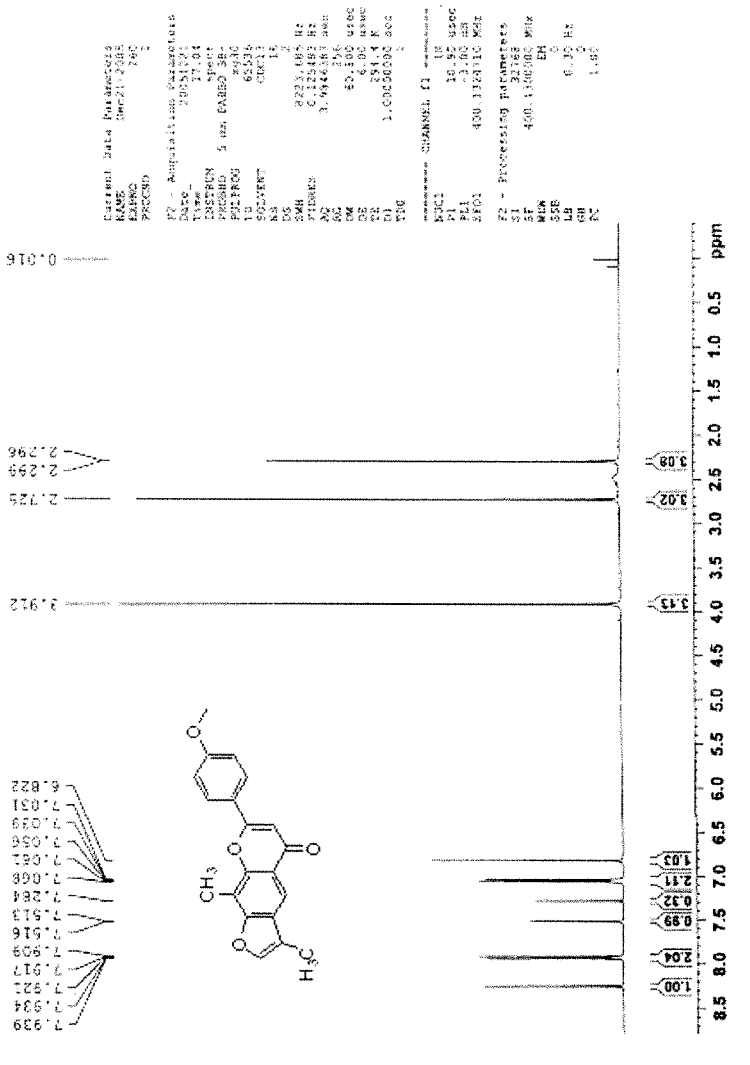


Figure 8: ^{1}H NMR of compound 7-(4-methoxy-phenyl)-3,9-dimethyl-furo[3,2-*g*]chromen-5-one **9a**.

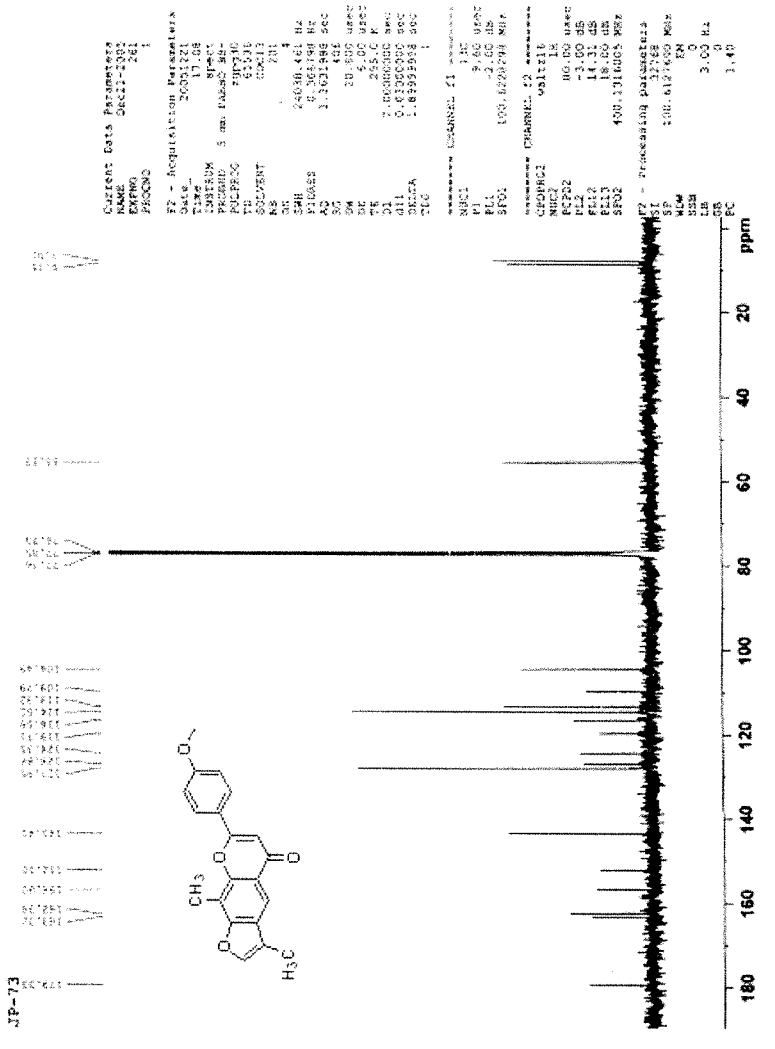


Figure 9: ^{13}C NMR of compound 7-(4-methoxy-phenyl)-3,9-dimethyl-furo[3,2-g]chromen-5-one **9a**.

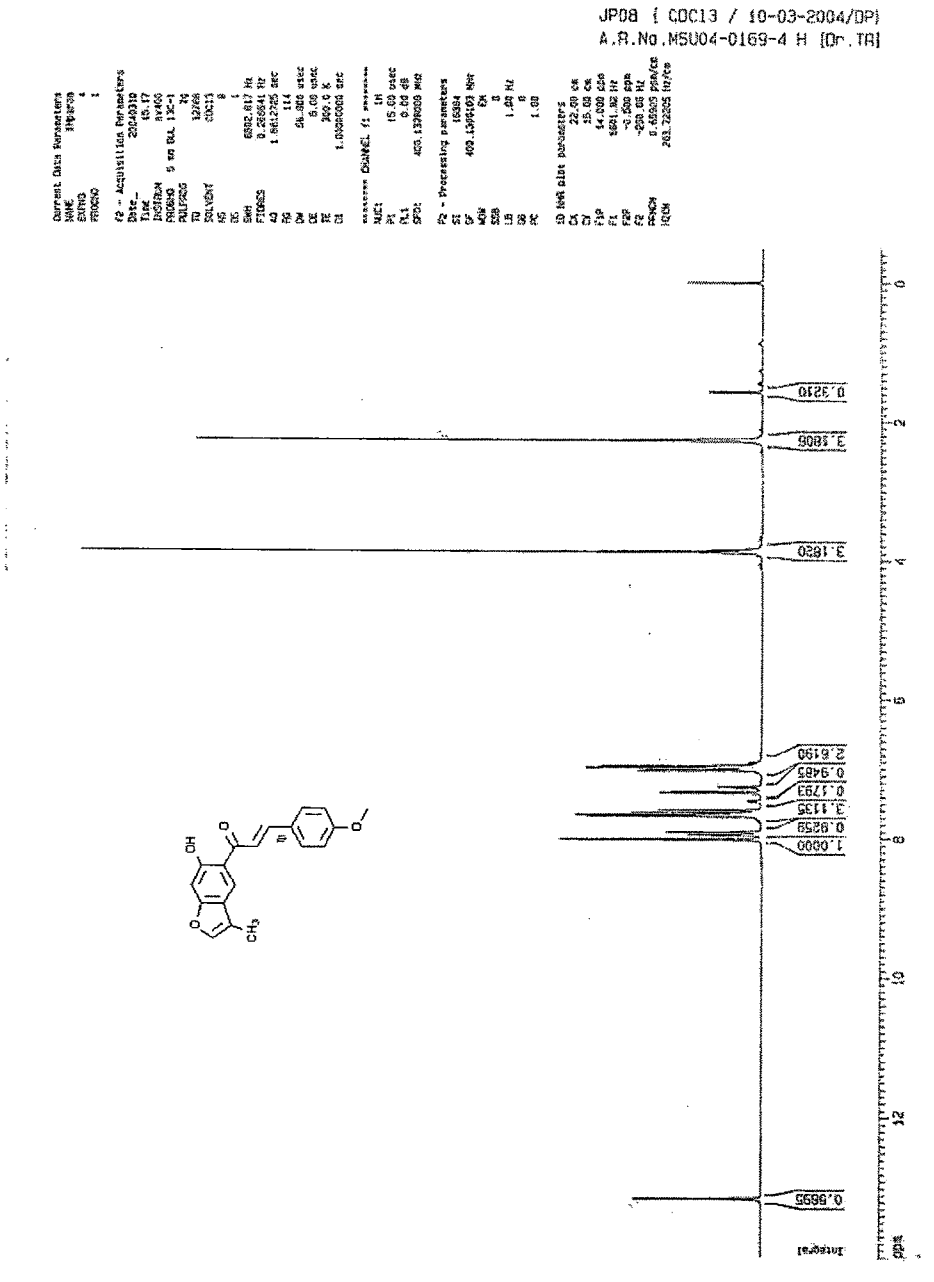


Figure 10: ^{1}H NMR of compound *E*-1-(6-hydroxy-3-methyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone **3b.**

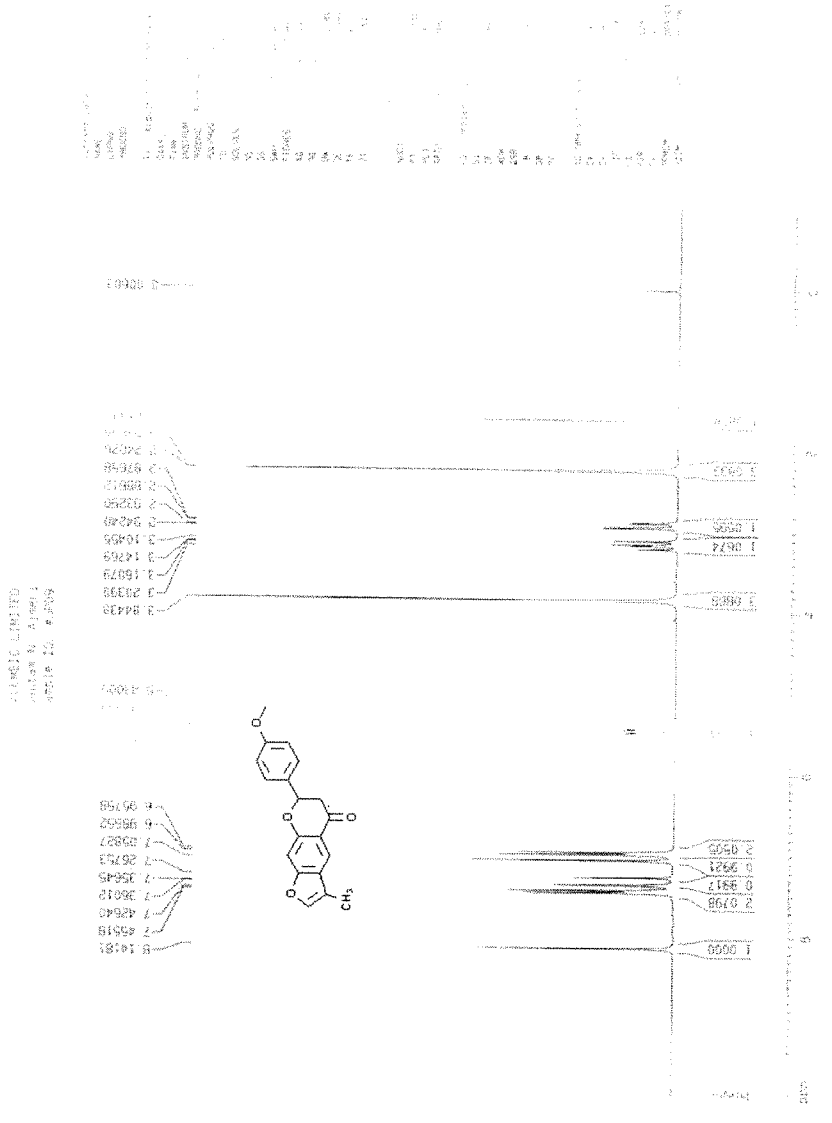


Figure 11: ^{1}H NMR of compound 7-(4-methoxy-phenyl)-3-methyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **6b.**

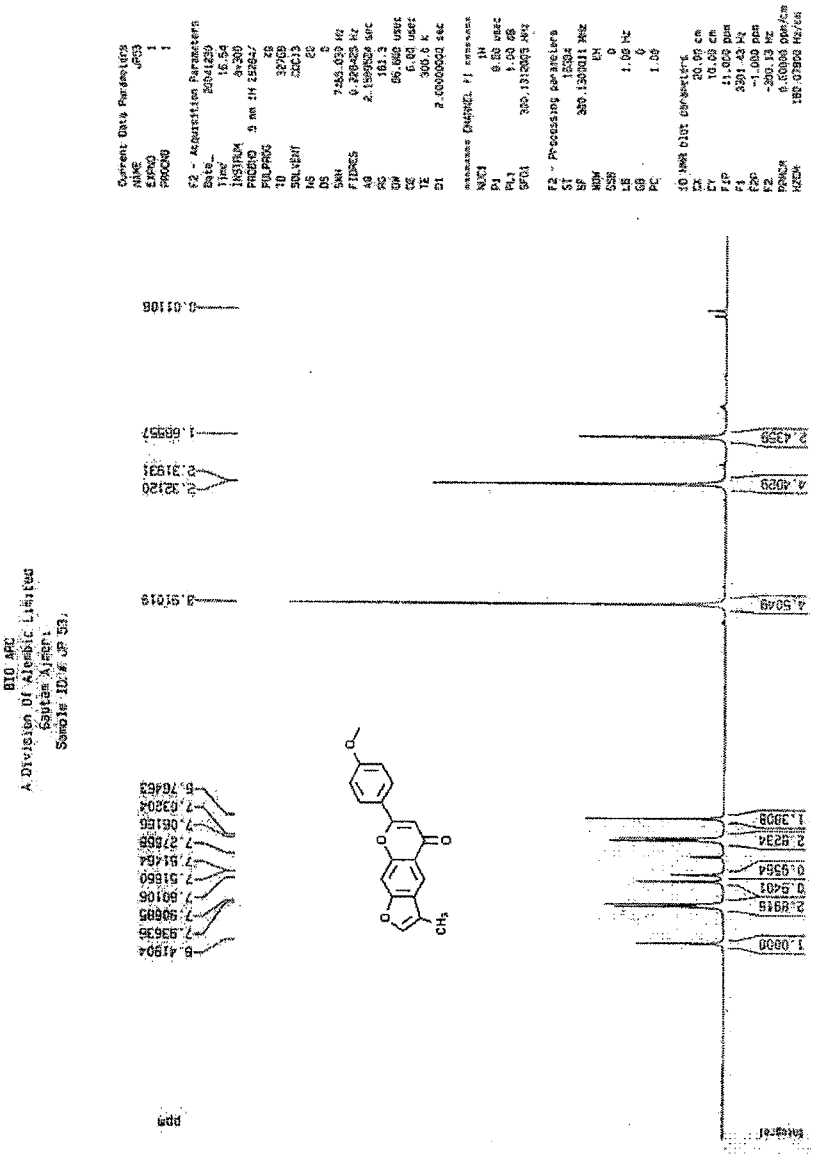


Figure 12: ^{1}H NMR of compound 7-(4-methoxy-phenyl)-3-methyl-furo[3,2-g]chromen-5-one **9b.**

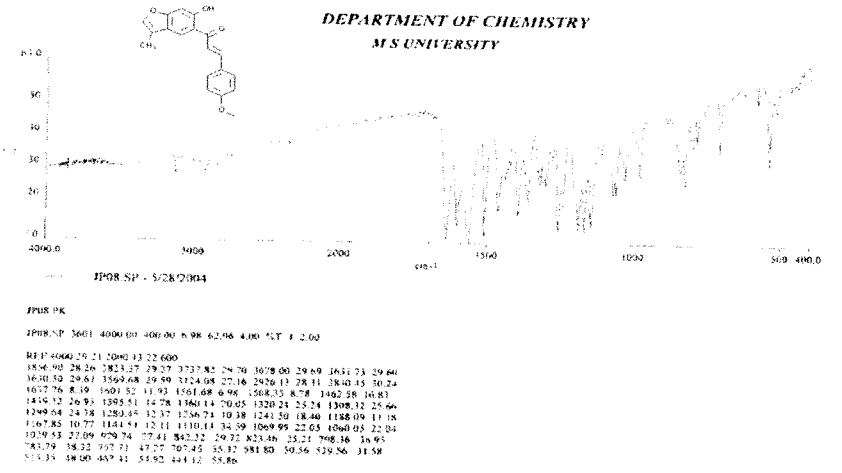


Figure 13: IR of compound *E*-1-(6-hydroxy-3-methyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone **3b.**

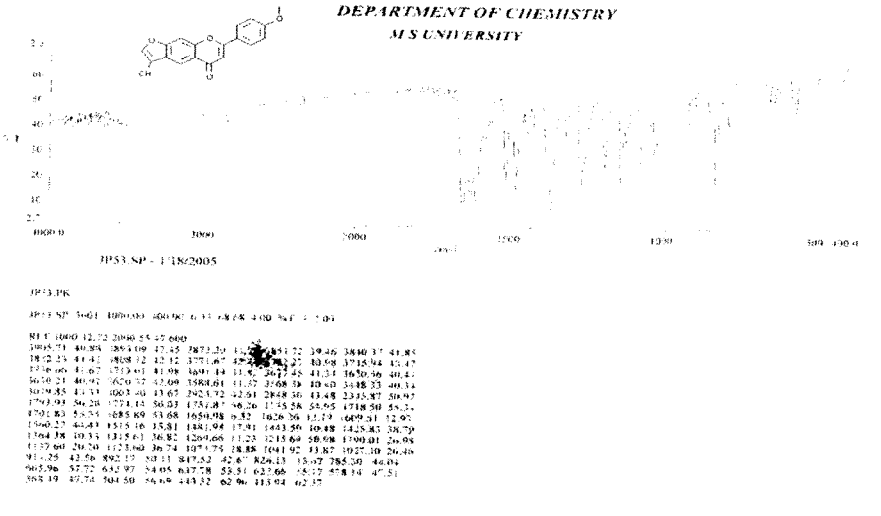
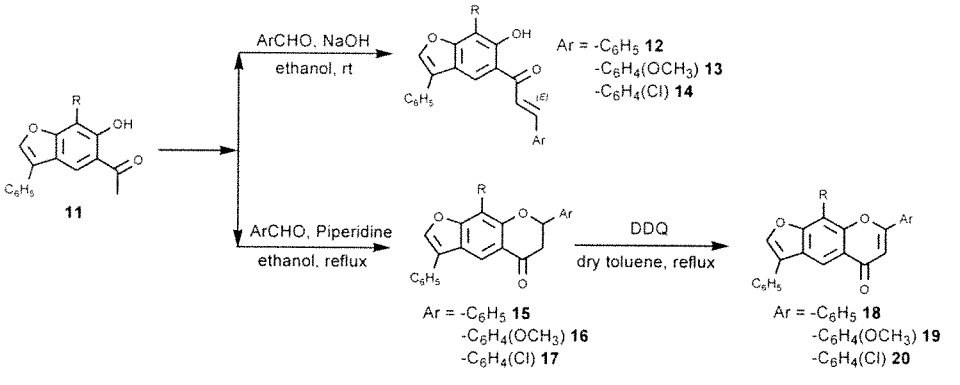


Figure 14: IR of compound 7-(4-methoxy-phenyl)-3-methyl-furo[3,2-*g*]chromen-5-one **9b.**



a = R = CH_3

b = R = H

Scheme 3

Similar series of reactions were carried out for 1-(6-hydroxy-7-methyl-3-phenylbenzofuran-5-yl)-ethanone **11a** and 1-(6-hydroxy-3-phenylbenzofuran-5-yl)-ethanone **11b** as shown in **Scheme 3**.

The ^{1}H NMR and mass spectrum (LCMS) of compound 3,7-diphenyl-furo[3,2-g]chromen-5-one **18b** obtained using mobile phase Acetonitrile: Ammonium acetate 1mM (90:10 % v/v) are shown in **Figure 15** and **Figure 16** respectively, which confirmed the formation of flavone. The ^{1}H NMR of **20a** is shown in **Figure 17**.

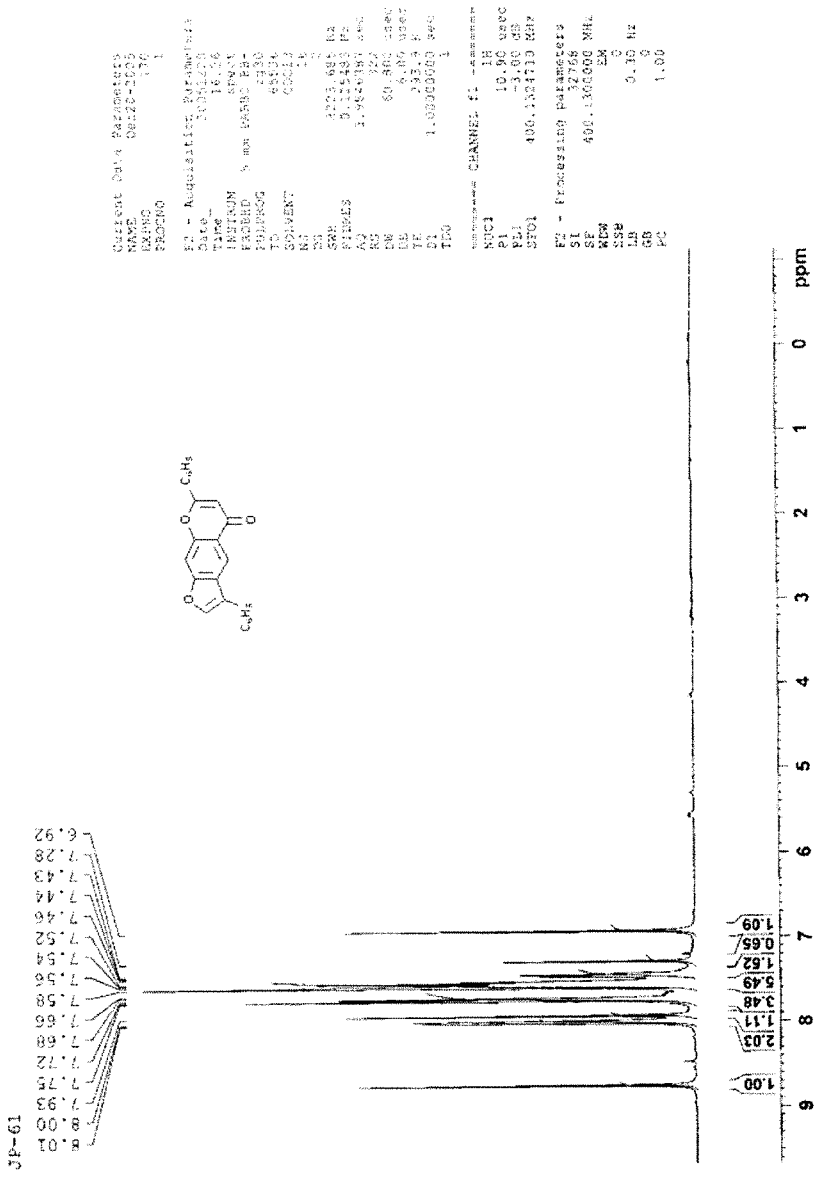


Figure 15: ^{1}H NMR of compound 3,7-diphenyl-furo[3,2-*g*]chromen-5-one **18b.**

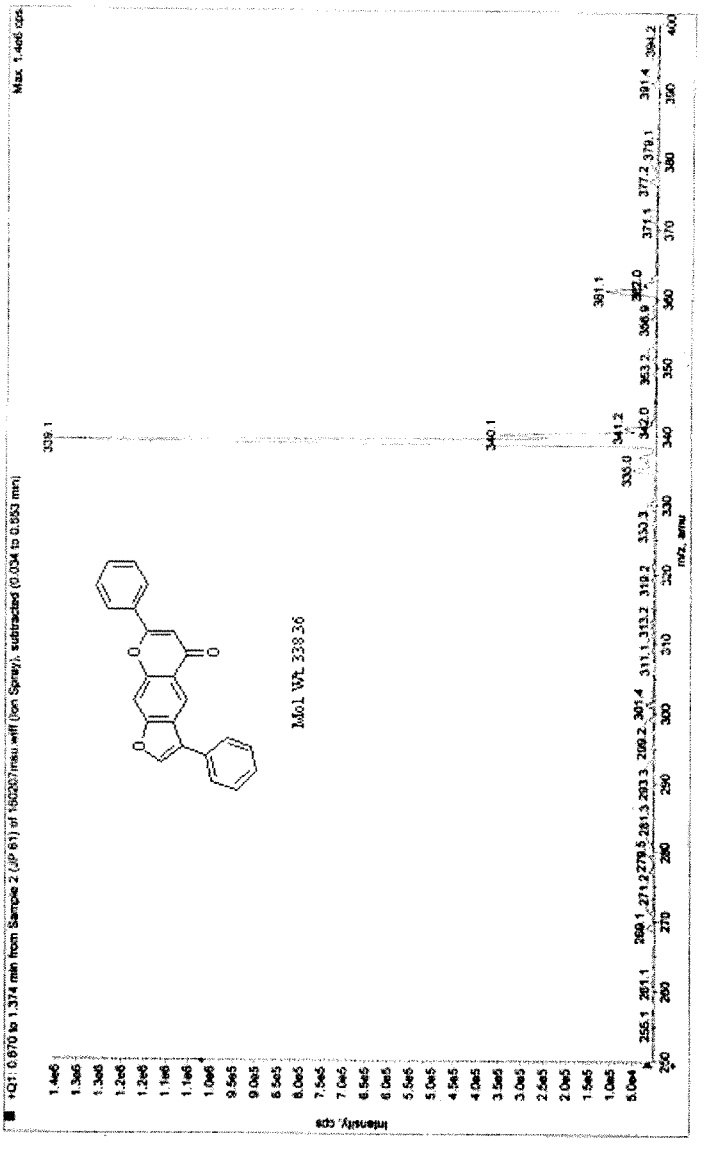


Figure 16: LCMS of compound 3,7-diphenyl-furo[3,2-*g*]chromen-5-one **18b**.

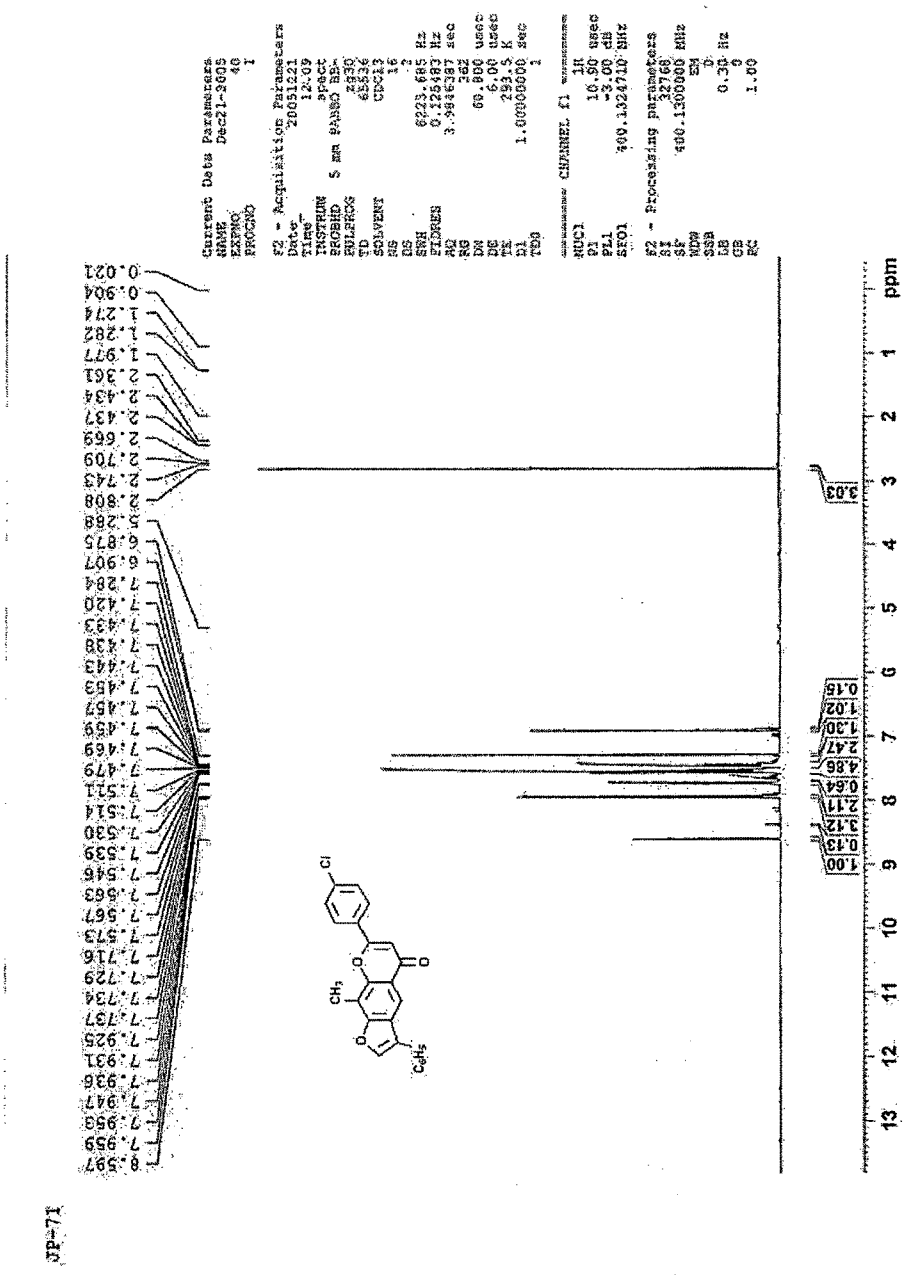
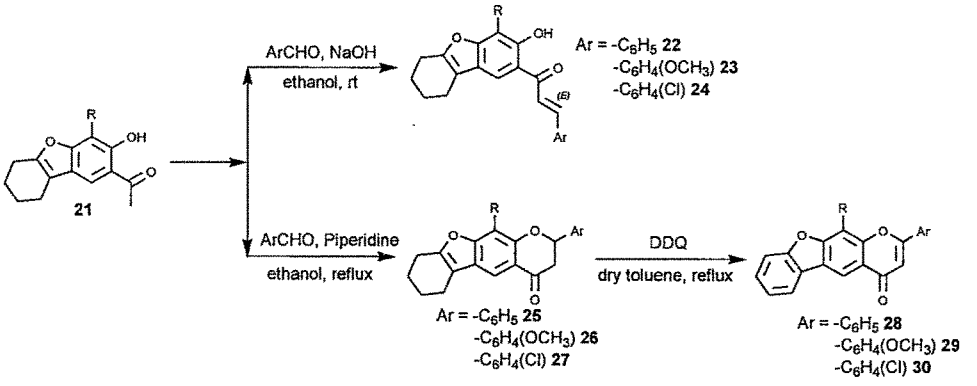


Figure 17: ^{1}H NMR of compound 7-(4-chloro-phenyl)-9-methyl-3-phenyl-furo[3,2-*g*]chromen-5-one **20a**



a = R = CH_3

b = R = H

Scheme 4

Similar series of reactions were carried out for 1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydrodibenzofuran-2-yl)-ethanone **21a** and 1-(3-hydroxy-6,7,8,9-tetrahydrodibenzofuran-2-yl)-ethanone **21b** as shown in **Scheme 4**. The ^{1}H NMR of **24a** and **25a** is shown in **Figure 18** and **Figure 19**.

In compounds **(28, 29 and 30)** the cyclohexane ring was also dehydrogenated along with flavanone ring, which was confirmed by the disappearance of multiplets of the cyclohexane ring in ^{1}H NMR spectra **(Figure 20)**.The ^{1}H NMR of **27b** is shown in **Figure 21**.

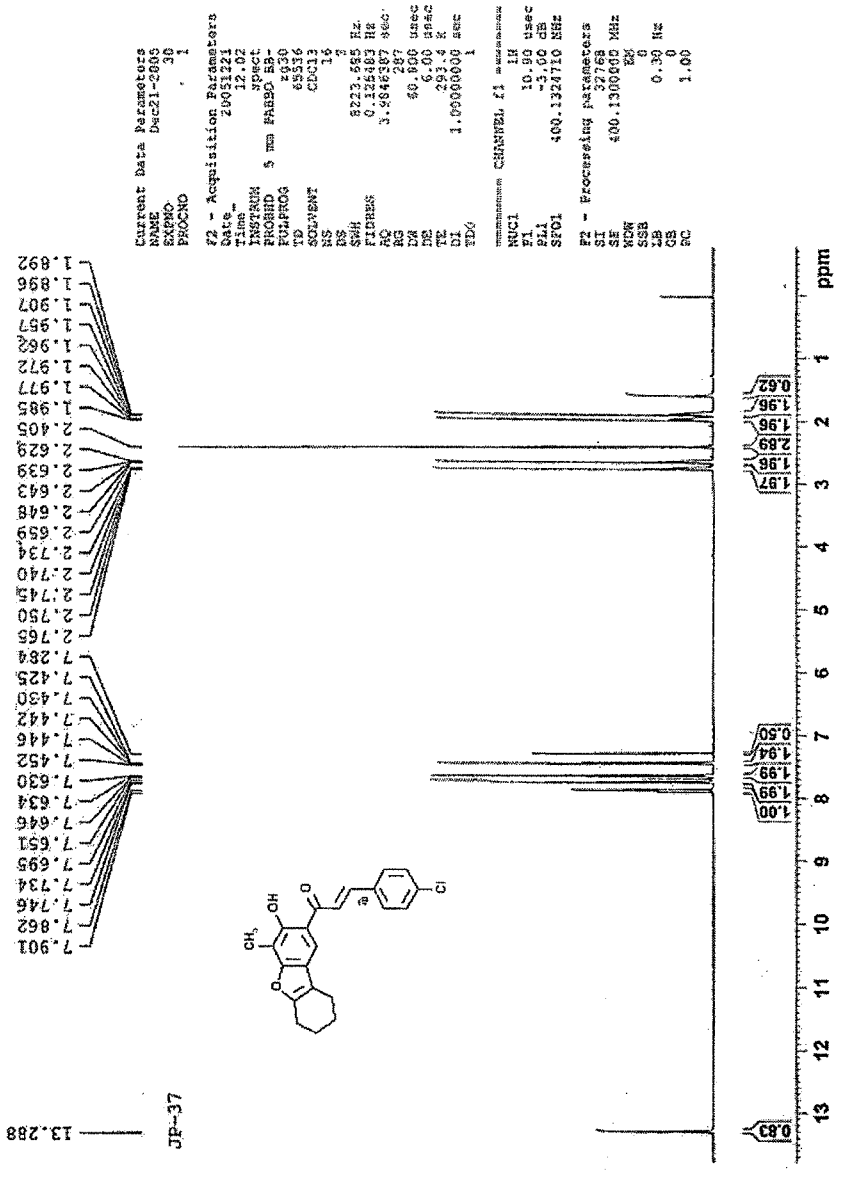


Figure 18: ^{1}H NMR of compound *E*-3-(4-chloro-phenyl)-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-propenone **24a.**

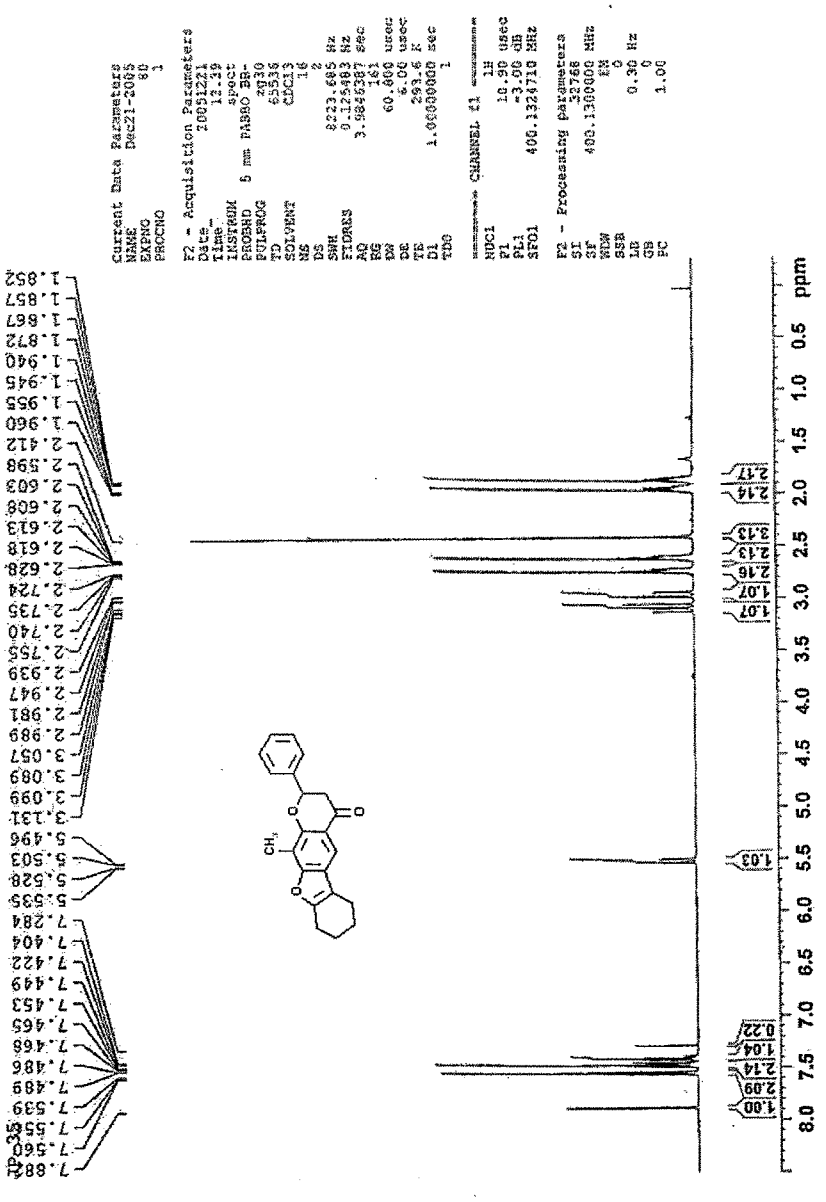


Figure 19: ^{1}H NMR of compound 10-methyl-8-phenyl-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one **25a.**

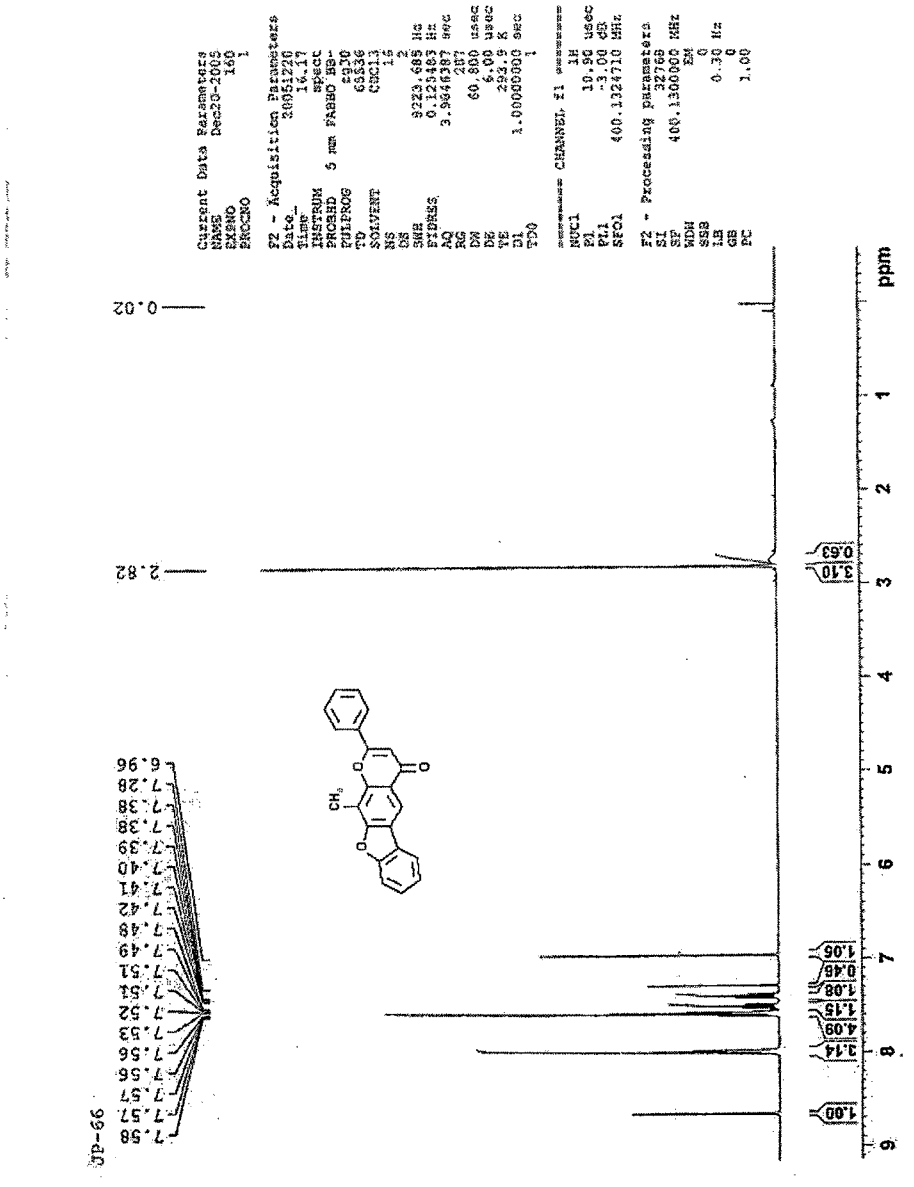


Figure 20: ^{1}H NMR of compound 10-methyl-8-phenyl-9,11-dioxa-benzo[*b*]fluoren-6-one **28a.**

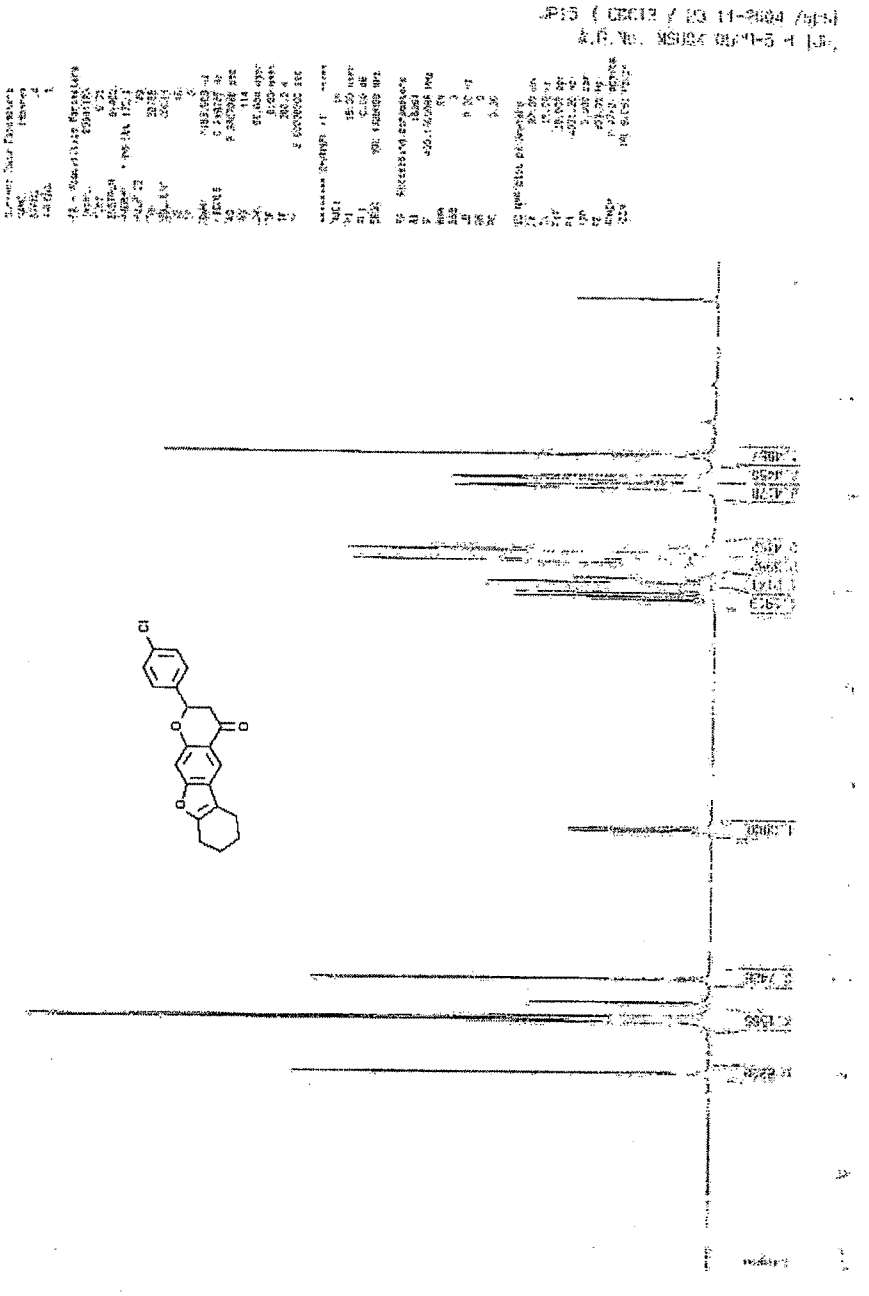
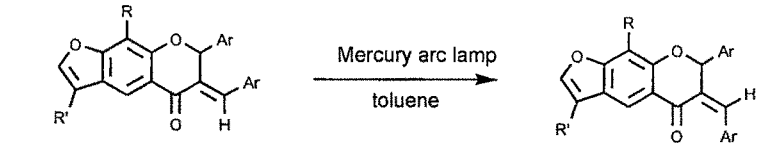


Figure 21: ^{1}H NMR of compound 8-(4-chloro-phenyl)-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one **27b.**

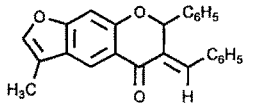


E-3 Arylidene flavanones

R = H, R' = -CH_3, Ar = -C_6H_5 **31**
R = H, R' = -CH_3, Ar = -C_6H_4(Cl) **32**
R = -CH_3, R' = -CH_3, Ar = -$C_6H_4(OCH_3)$ **33**
R = -CH_3, R' = -C_6H_5, Ar = -$C_6H_4(OCH_3)$ **34**

Z-3 Arylidene flavanones

R = H, R' = -CH_3, Ar = -C_6H_5 **35**



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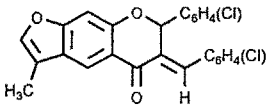

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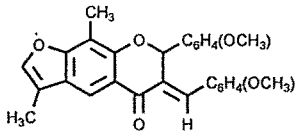

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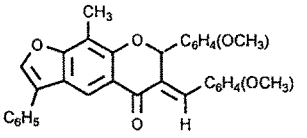

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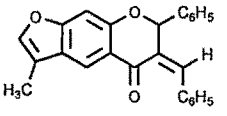


35

Scheme 5: Photoisomerization of *E*-3 Arylidene flavanones to *Z*-3 Arylidene flavanones.

When excess of arylaldehyde was used in the preparation of flavanones from *ortho*- hydroxy acetyl benzofurans **(1, 11 and 21)** using piperidine, it was observed that along with flavanones, 3-arylidene flavanones were also formed **(31-34)**. They were isolated by column chromatography and characterized for some reactions. When two moles of aryl aldehyde was condensed with one mole of *ortho*-hydroxy acetyl benzofuran in presence of piperidine, 3-arylidene

flavanone was the major product obtained. Stereochemistry of 3-arylidene flavanones has been determined by carrying out synthesis of both *Z* and *E* diastereomers. When ^{1}H NMR spectrum for compound *E*-6-benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **31** was recorded in $CDCl_3$ **(Figure 22)**, two singlets at δ 6.6 ppm and 8.1 ppm for one proton each indicated C(2)H flavanone proton and vinylic proton respectively. This shows the formation of 3-arylidene flavanones in *E* configuration since the vinylic proton is deshielded due to the diamagnetic anisotropy of the carbonyl group.[15] The *E* configuration of 3-arylidene flavanone was further confirmed by converting compound **31** into its *Z* isomer **35** photochemically, using mercury arc 150W lamp and toluene as solvent **(Scheme 5)**. Compound *Z*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **35** was purified by column chromatography using neutral alumina, as silica gel showed some conversion back into the *E* isomer. The ^{1}H NMR of compound **35** in $CDCl_3$ **(Figure 23)** showed two singlets at δ 6.15 and 6.7 ppm for one proton each indicating C(2)H flavanone proton and vinylic proton respectively. Since the vinylic proton is now shielded, it confirmed compound **35** to be in *Z* configuration. However, the allylic coupling between C(2)H flavanone proton and the vinylic proton could not be resolved in the ^{1}H NMR spectra. It was further supported by the IR absorption band of carbonyl group at 1670cm^{-1}(*s*) for the *E* isomer **(Figure 24)** and at 1661 cm^{1}(*s*) for the *Z* isomer **(Figure 25)**. The absorption bands at 1624cm^{-1}(*s*) and 1604cm^{-1}(*s*) indicated furan ring (-C=C-) stretching and alkene (-C=C-) stretching respectively in both *E* and *Z* isomers. The UV spectrum in ethanol showed absorption at 309, 257.41 and 227nm for the *E* isomer and 306, 248.83 and 227nm for the *Z* isomer.

The probable mechanism for the formation of flavanone using piperidine is shown in **Scheme 6**, whereas; the mechanism for the formation of 3-arylidene flavanone is shown in **Scheme 7**. The structures of all the compounds have been established on the basis of their elemental analyses and spectral data (IR, NMR).

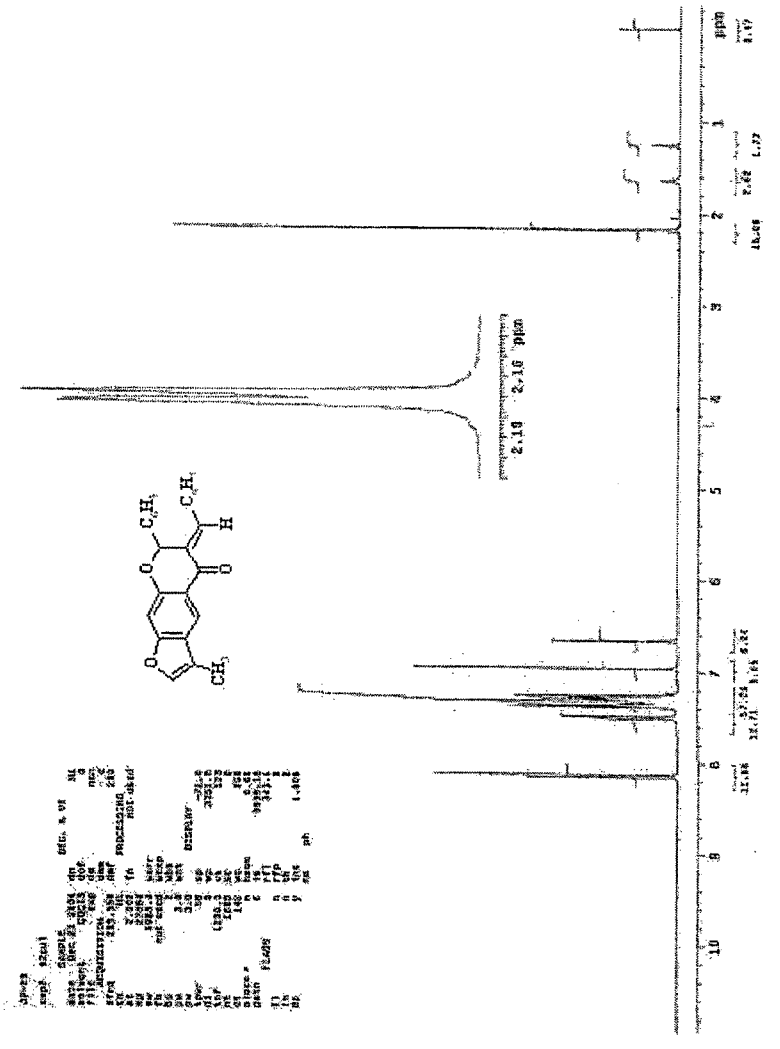


Figure 22: ^{1}H NMR spectrum of compound *E*-6-benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **31**.

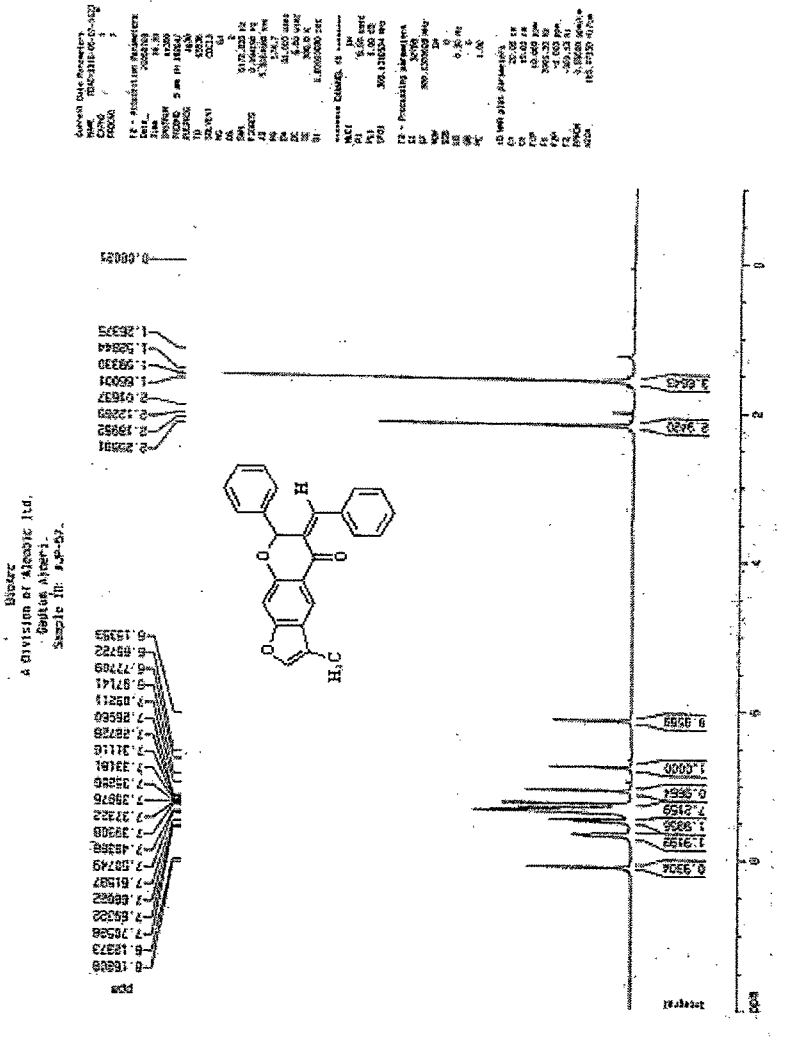


Figure 23: ^{1}H NMR spectrum of compound *Z*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **35.**

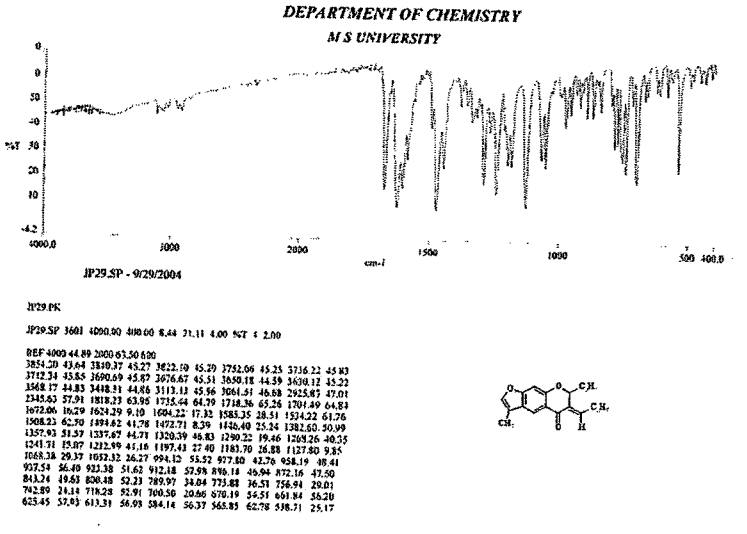


Figure 24: IR spectrum of compound *E*-6-benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **31**.

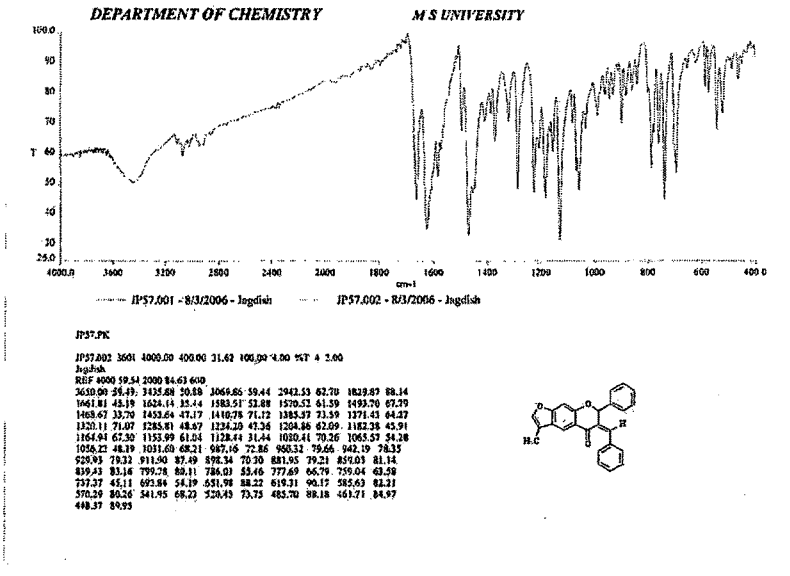
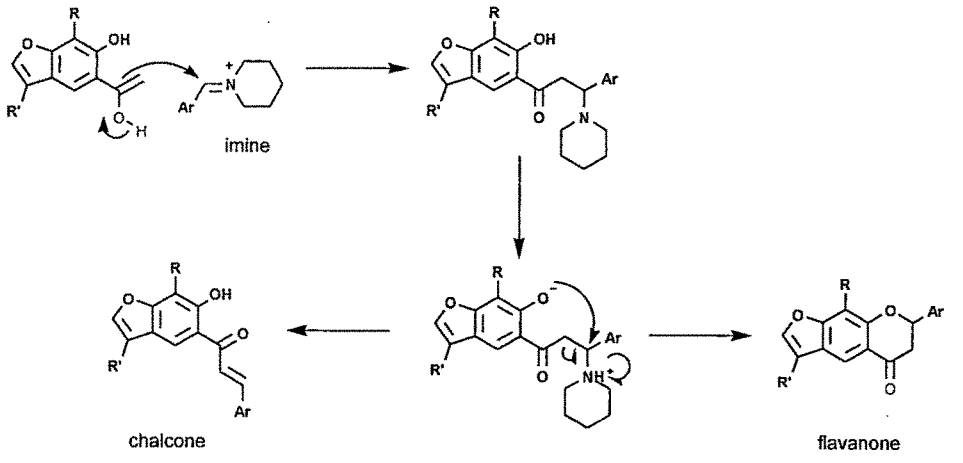
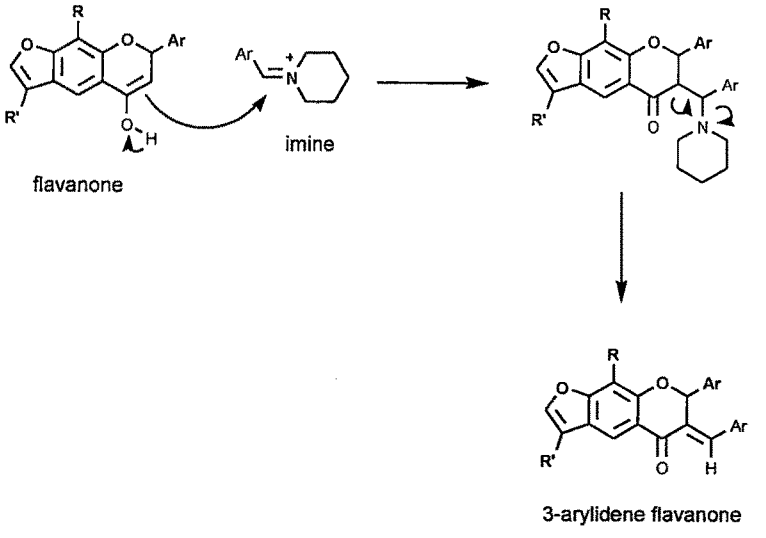


Figure 25: IR spectrum of compound *Z*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **35.**



Scheme 6: Probable mechanism for the formation of flavanones using piperidine.



Scheme 7: Probable mechanism for the formation of 3-arylidene flavanones.

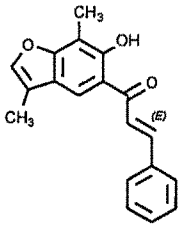
Physiological activity

Flavonoids have potential applications as pharmaceutical drugs. Some of the compounds have been screened for possible physiological properties.

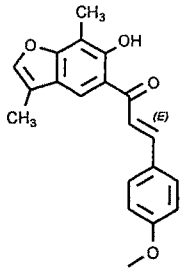
DNA Topoisomerase inhibition

Some of the compounds were tested for the DNA Topoisomerase inhibitory activity against filarial parasites at 20 μg per reaction mixture. None of the compounds tested (**5a, 8a, 10b, 11b, 12b, 13b, 16b, 19b, 25a, 33**) have any activity against the enzyme.

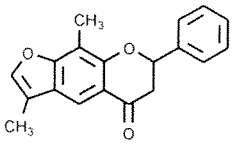
However, some of the compounds **(2a, 3a, 5a, 18b)** showed complex formation with DNA, which indicates that the compound can be explored for antimicrobial activity. The results are shown in **Table 1**.



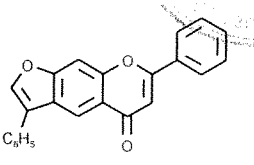
E-1-(6-hydroxy-3,7-dimethyl-benzofuran benzofuran-5-yl)-3-phenyl-propenone **2a**



E-1-(6-hydroxy-3,7-dimethyl--5-yl)-3-(4-methoxy-phenyl)-propenone **3a**



3,9-dimethyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **5a**



3,7-diphenyl-furo[3,2-*g*]chromen-5-one **18b**

Table 1

Compound	DNA Topoisomerase inhibition	Complex formation with DNA
23b	-	-
13b	-	-
2a	-	✓
3a	-	✓
4a	-	-
25a	-	-
15a	-	-
5a	-	✓
18b	-	✓
33	-	-

Non Steroidal Anti-inflammatory activity

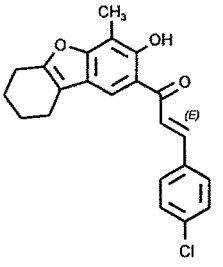
Two of the compounds, *E*-3-(4-chloro-phenyl)-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-propenone **24a** and 7-(4-chloro-phenyl)-9-methyl-3-phenyl-furo[3,2-*g*]chromen-5-one **20a** were tested for anti-inflammatory activity. The results are shown in **Table 2**.

Methodology: Sprague-Dawley (Male/Female) rats weighing 150-250g were used for the edema test. They were divided into two groups. Rats were deprived of food but not of water for 18 hours prior to the experiment. The test compounds

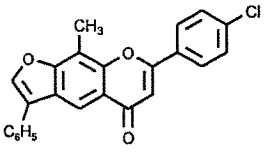
were administered orally (50 mg/Kg) using a blunt-tipped needle as a suspension using 0.1% sodium CMC (Carboxy Methyl Cellulose) as vehicle and control group is given only vehicle. One hour later, 0.1ml of 1% Carrageenan solution in saline was injected in the sub plantar region of the right hind paw of each rat. After 5 minutes of the carrageenan administration, the displacement in the mercury, in mercury filled Plethysmometer by the treated paw was observed by dipping the treated paw up to the premarked ankle, which was the 0 hour reading. After 3 hours the reading were repeated which were the final reading.[16]

The increase of rat paw volume after 3 hours was calculated as percentage compared with the volume measured immediately after injection of the irritant for each animal. The difference of average values between treated animals and control groups is calculated for each time and statistically evaluated.[16]

Compound **24a** (chalcone) showed better percentage protection at 50mg/Kg dose compared to **20a** (flavone) using positive control-Ibuprofen.



E-3-(4-chloro-phenyl)-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-propenone **24a**



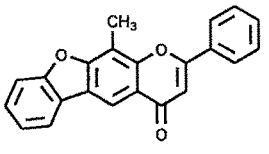
7-(4-chloro-phenyl)-9-methyl-3--phenyl-furo[3,2-*g*] chromen-5-one **20a**

Table 2

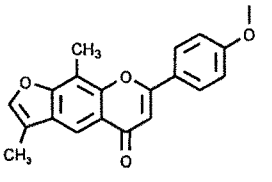
Compound	% Protection	Dose (mg/Kg)
24a	38	50
20a	24	50
Positive control (Ibuprofen)	32	50

Antioxidant activity

Evaluation of free radical scavenging activity of compounds in one *in-vitro* model was done.[17] Compounds 10-methyl-8-phenyl-9,11-dioxa-benzo[*b*]fluoren-6-one **28a** and 7-(4-methoxy-phenyl)-3,9-dimethyl-furo[3,2-*g*]chromen-5-one **9a** were dissolved separately in methanol and suitable dilutions of it were used in testing. The samples did not show DPPH radical scavenging activity upto a concentration of 1mg of the sample tried. (EC_{50} of Pyrogallol used as positive control was 4.85μg).



10-methyl-8-phenyl-9,11-dioxa-benzo[*b*]fluoren-6-one **28a**



7-(4-methoxy-phenyl)-3,9-dimethyl-furo[3,2-*g*]chromen-5-one **9a**

Anticancer activity

Compounds 7-(4-chloro-phenyl)-3-methyl-furo[3,2-*g*]chromen-5-one **10b** and 3,7-diphenyl-furo[3,2-*g*]chromen-5-one **18b** were evaluated for *in-vitro*

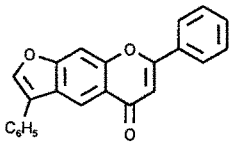
cytotoxicity against human cancer cell lines. The human cancer cell lines produced from National Cancer Institute, Frederick, U.S.A. were used in present study. Cells were grown in tissue culture flasks in complete growth medium (RPMI-1640 medium with 2 m*M* glutamine, 100 μg/ml streptomycin, pH 7.4, sterilized by filtration and supplemented with 10 % fetal calf serum and 100 units/ml penicillin before use) at 37 °C in an atmosphere of 5 % CO_2 and 90 % relative humidity in a carbon dioxide incubator. The cells at subconfluent stage were harvested from the flask by treatment with trypsin (0.05 % in PBS containing 0.02 % EDTA) for determination of cytotoxicity. Cells with viability of more than 98 %, as determined by trypan blue exclusion, were used for assay. The cell suspension of 1 x 10^5 cells/ml was prepared in complete growth medium for determination of cytotoxicity.

Stock solutions of 2 x 10^{-2} *M* of **10b** and **18b** were prepared in DMSO. The stock solutions were serially diluted with complete growth medium containing 50 μg/ml of gentamycin to obtain working test solutions of required concentrations.

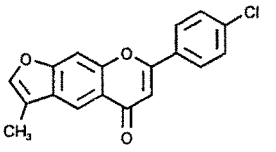
In-vitro cytotoxicity against six human cancer cell lines was determined by two different experiments, using 96-well tissue culture plates. The 100 μl of cell suspension was added to each well of the 96-well tissue culture plate. The cells were incubated for 24 hours. Test materials in complete growth medium (100 μl) were added after 24 hours incubation to the wells containing cell suspension. The plates were further incubated for 48 hours (at 37 °C in an atmosphere of 5 % CO_2 and 90 % relative humidity in a carbon dioxide incubator) after addition of test material and then the cell growth was stopped by gently layering trichloroacetic acid (50 % TCA, 50 μl) on top of the medium in all the wells. The plates were incubated at 4 °C for one hour to fix the cells attached to the bottom of the wells. The liquid of all the wells was gently pipetted out and discarded. The plates were washed five times with distilled water to remove TCA, growth medium low molecular weight metabolites, serum proteins etc. and air-dried. Cell growth was measured by staining with Sulforhodamine B dye. The adsorbed dye was

dissolved in Tris-Buffer (100 µl, 0.01 *M*, pH 10.4) and plates were gently shaken for 10 minutes on a mechanical shaker. The optical density (OD) was recorded on ELISA reader at 540 nm. The cell growth was calculated by subtracting mean OD value of respective blank from the mean OD value of experiment set. Percent growth in presence of test material was calculated considering the growth in absence of any test material as 100 % and in turn percent growth inhibition in presence of test material was calculated.

Compound **18b** showed 74 % growth inhibition against Breast MCF-7 cell line and 40 % growth inhibition against Prostate DU-145 cell line at $1x10^{-4}$ concentrations. 5FU, Mito-C, Paclitaxel and Adriamycin are the standard drugs used. The results are tabulated in **Table 3**.



3,7-diphenyl-furo[3,2-*g*] chromen-5-one **18b**



7-(4-chloro-phenyl)-3-methyl-furo [3,2-*g*]chromen-5-one **10b**

Table 3

Cell Line Type		Colon	Colon	Colon	Prostate	Liver	Breast
Cell line		502713	HT-29	SW-620	DU-145	HEP-2	MCF-7
Compound	Conc. (M)	Growth Inhibition (%)					
10b	$1X10^{-6}$	0	10	0	3	-	-
	$1X10^{-5}$	0	12	0	8	0	6
	$1X10^{-4}$	-	-	0	11	3	30
18b	$1X10^{-6}$	0	5	0	0	-	-
	$1X10^{-5}$	0	6	29	5	15	35
	$1X10^{-4}$	-	-	32	40	30	74
5FU	$5X10^{-5}$	25	36	41	31	-	-
Mito-C	$1X10^{-5}$	84	63	67	79	-	65
Paclitaxel	$1X10^{-5}$	26	76	41	-	-	-
Adriamycin	$1X10^{-6}$	-	-	-	67	47	78

3.A.3 Experimental

^{1}H and ^{13}C NMR spectra were recorded on Brucker 300MHz spectrophotometer except where mentioned. Chemical shifts are given in δ ppm downfield from tetramethylsilane as internal standard. Infrared spectra were recorded on a Perkin-Elmer FT-IR spectrometer (spectrum RX1) using KBr optics. UV spectra were recorded on Perkin Elmer Lambda 35 UV/Vis spectrophotometer. Elemental analyses were carried out on Perkin-Elmer C, H, N, S analyzer (Model-2400). The mass spectrum was obtained on Perkin-Elmer Sciex Triple Quadrupole LC/MS/MS Mass Spectrometer (Model-016932) using Ion Spray source. Melting points are uncorrected and were determined using a scientific capillary melting point apparatus. Purity of the compounds was checked by TLC on Acme's silica gel G plates using UV/I_2 vapour as visualizing agent. Acme's silica gel (60-120 mesh) and neutral alumina powder was used for column chromatographic purification.

General procedure for chalcones (2-4, 12-14, 22-24).

***E*-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-3-phenyl-propenone 2a.** A mixture of 1-(6-hydroxy-3,7-dimethylbenzofuran-5-yl)-ethanone **1a** (0.00625 moles) and freshly distilled benzaldehyde (0.00625 moles) in ethanolic sodium hydroxide solution (50 cm^3, 1 %) was stirred for 8 h at room temperature. The excess of ethanol was distilled off *in vacuo* and the reaction mixture was poured into ice-hydrochloric acid and filtered. The product was purified by column chromatography using petroleum ether (60-80 °C): ethyl acetate mixture (9:1) as eluent to give *E*-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-3-phenyl-propenone **2a** (77 %) as orange crystals; mp 113-114°C; (Found: C, 78.12; H, 5.55. $C_{19}H_{16}O_3$ (292.33) requires C, 78.06; H, 5.51 %); υ_{max}/cm^{-1} 3445, 3115, 2956, 1644, 1566, 1528, 1209 and 1163; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.29 (3H, d, *J* 1.2, C(3)CH_3), 2.48 (3H, s, C(7)CH_3), 7.34 (1H, d, *J* 1.2, C(2)H), 7.46-7.49 (3H, m, C(3')H,

C(4')H, C(5')H), 7.70-7.75 (1H, d , *J* 15.6, C(α)H), 7.73-7.74 (2H, m, C(2')H and C(6')H), 7.94-7.99 (1H, d, *J* 15.6, C(β)H), 8.1 (1H, s, C(4)H) and 13.1 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-3-methyl-benzofuran-5-yl)-3-phenyl-propenone 2b.** 81 %; orange crystals; mp 127-128 °C; (Found: C, 77.59; H, 5.01. $C_{18}H_{14}O_3$ (278.30) requires C, 77.68; H, 5.07 %); υ_{max}/cm^{-1} 3437, 3110, 2986, 1632, 1556, 1521, 1217 and 1164; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.27 (3H, d, *J* 1.1, C(3)CH_3), 7.02 (1H, s, C(7)H), 7.34 (1H, d, *J* 1.1, C(2)H), 7.45-7.47 (3H, m, C(3')H, C(4')H, C(5')H), 7.70-7.75 (1H, d, *J* 15.5, C(α)H), 7.71-7.72 (2H, m, C(2')H and C(6')H), 7.92-7.97 (1H, d, *J* 15.5, C(β)H), 8.01 (1H, s, C(4)H) and 13.05 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone 3a.** 51 %; orange crystals; mp 144-145 °C; (Found: C, 74.21; H, 5.34. $C_{20}H_{18}O_4$ (322.35) requires C, 74.51; H, 5.62 %); υ_{max}/cm^{-1} 3441, 3121, 2923, 1631, 1601, 1590, 1560, 1518, 1181, 1163 and 1149; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.28 (3H, d, *J* 1.2, C(3)CH_3), 2.41 (3H, s, C(7)CH_3), 3.89 (3H, s, C(4')OCH_3), 6.976-6.998 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.38 (1H, d, *J* 1.2, C(2)H), 7.63-7.67 (1H, d, *J* 15.6, C(α)H), 7.673-7.695 (2H, d, *J* 8.8, C(2')H and C(6')H), 7.904 (1H, s, C(4)H), 7.921-7.960 (1H, d, *J* 15.6, C(β)H) and 13.418 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-3-methyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone 3b.** 55 %; orange crystals; mp 127-129 °C; (Found: C, 73.71; H, 4.93. $C_{19}H_{16}O_4$ (308.33) requires C, 74.01; H, 5.23 %); υ_{max}/cm^{-1} 3452, 3124, 2926, 1637, 1601, 1561, 1508, 1188, 1167 and 1144; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.26 (3H, d, *J* 1.1, C(3)CH_3), 3.89 (3H, s, C(4')OCH_3), 6.95-6.97 (2H, d, *J* 8.44, C(3')H and C(5')H), 7.01 (1H, s, C(7)H), 7.33 (1H, d, *J* 1.1, C(2)H), 7.58-7.62 (1H, d, *J*

15.32, C(α)H), 7.65-7.67 (2H, d, *J* 8.44, C(2')H and C(6')H), 7.90-7.94 (1H, d, *J* 15.32, C(β)H), 8.01 (1H, s, C(4)H) and 13.14 (1H, s, C(6)OH chelated).

***E*-3-(4-chloro-phenyl)-1-(6-hydroxy-3,7-dimethyl-benzofuran-5-yl)-propenone 4a.** 74.5 %; orange crystals; mp 206-207 °C; (Found: C, 69.57; H, 4.60. $C_{19}H_{15}O_3Cl$ (326.77) requires C, 69.83; H, 4.62 %); υ_{max}/cm^{-1} 3458, 3114, 2916, 1633, 1609, 1556, 1500, 1178, 1163 and 1141; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.3 (3H, d, *J* 1.4, C(3)CH_3), 2.4 (3H, s, C(7)CH_3), 7.37 (1H, d, *J* 1.4, C(2)H), 7.42-7.44 (2H, d, *J* 8.4, C(3')H and C(5')H), 7.64-7.66 (2H, d, *J* 8.4, C(2')H and C(6')H), 7.70-7.74 (1H, d, *J* 15.48, C(α)H), 7.88-7.92 (1H, d, *J* 15.48, C(β)H), 8.05 (1H, s, C(4)H), 12.99 (1H, s, C(6)OH chelated); *m/z* 349 (M+23, 14%), 329.2 (M+2, 37), 327.1 (M+1, 100), 301.2 (11), 300.3 (26), 295.1 (20), 293.2 (17), 279.2 (9), 269.2 (6).

***E*-3-(4-chloro-phenyl)-1-(6-hydroxy-3-methyl-benzofuran-5-yl)-propenone 4b.** 68 %; orange crystals; mp 159-160 °C; (Found: C, 68.78; H, 3.98. $C_{18}H_{13}O_3Cl$ (312.75) requires C, 69.12; H, 4.18 %); υ_{max}/cm^{-1} 3444, 3122, 2916, 1629, 1611, 1569, 1511, 1178, 1156 and 1139; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.27 (3H, d, *J* 1.1, C(3)CH_3), 7.03 (1H, s, C(7)H), 7.35 (1H, d, *J* 1.1, C(2)H), 7.42-7.44 (2H, d, *J* 8.36, C(3')H and C(5')H), 7.63-7.65 (2H, d, *J* 8.36, C(2')H and C(6')H), 7.68-7.72 (1H, d, *J* 15.44, C(α)H), 7.88-7.91 (1H, d, *J* 15.44, C(β)H), 8.00 (1H, s, C(4)H), 12.97 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-7-methyl-3-phenyl-benzofuran-5-yl)-3-phenyl-propenone 12a.** 85.5%; orange crystals; mp 188-189 °C; (Found: C, 81.16; H, 4.81. $C_{24}H_{18}O_3$ (354.40) requires C, 81.33; H, 5.11%); υ_{max}/cm^{-1} 3437, 2932, 1638, 1588, 1556, 1500, 1451, 1386, 1255 and 1175; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.48 (3H, s, C(7)CH_3), 7.44-7.74 (12H, m, C(2)H, C(α)H, C(2')H to C(6')H, C(2'')H to C(6'')H), 7.96-8.00 (1H, d, *J* 15.6, C(β)H), 8.19 (1H, s, C(4)H) and 13.31 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-3-phenyl-benzofuran-5-yl)-3-phenyl-propenone 12b.** 89 %; orange crystals; mp 159-160 °C; (Found: C, 80.52; H, 4.40. $C_{23}H_{16}O_3$ (340.37) requires C, 81.16; H, 4.73%); υ_{max}/cm^{-1} 3433, 2933, 1639, 1611, 1555, 1511, 1467, 1376, 1247 and 1135; δ_H (300 MHz; $CDCl_3$; Me_4Si) 7.12 (1H, s, C(7)H), 7.43-7.69 (12H, m, C(α)H, C(2)H, C(2')H to C(6')H, C(2'')H to C(6'')H), 7.93-7.99 (1H, d, *J* 15.38, C(β)H), 8.30 (1H, s, C(4)H), and 13.03 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-7-methyl-3-phenyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone 13a.** 61 %; orange crystals; mp 210-212 °C; (Found: C, 77.82; H, 5.03. $C_{25}H_{20}O_4$ (384.42) requires C, 78.10; H, 5.24%); υ_{max}/cm^{-1} 3441, 3110, 2946, 1644, 1615, 1560, 1522, 1201 and 1177; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.49 (3H, s, C(7)CH_3), 3.89 (3H, s, C(4'')OCH_3), 6.95-6.97 (2H, d, *J* 8.5, C(3'')H and C(5'')H), 7.43-7.47 (1H, m, C(4')H), 7.53-7.57 (1H, d, *J* 15.3, C(α)H), 7.56-7.59 (2H, d, *J* 8.48, C(2'')H and C(6'')H), 7.62-7.64 (4H, m, C(2')H, C(3')H, C(5')H, C(6')H), 7.70 (1H, s, C(2)H), 7.93-7.97 (1H, d, *J* 15.3, C(β)H), 8.33 (1H, s, C(4)H) and 13.19 (1H, s, C(6)OH chelated).

***E*-1-(6-hydroxy-3-phenyl-benzofuran-5-yl)-3-(4-methoxy-phenyl)-propenone 13b.** 59.5 %; orange crystals; mp 175-177 °C; (Found: C, 77.98; H, 4.91. $C_{24}H_{18}O_4$ (370.40) requires C, 77.82; H, 4.89%); υ_{max}/cm^{-1} 3449, 3113, 2926, 1639, 1605, 1567, 1512, 1207 and 1172; δ_H (400 MHz; $CDCl_3$; Me_4Si) 3.87 (3H, s, C(4'')OCH_3), 6.94-6.96 (2H, d, *J* 8.48, C(3'')H and C(5'')H), 7.12 (1H, s, C(7)H), 7.42-7.46 (1H, m, C(4')H), 7.53-7.57 (1H, d, *J* 15.28, C(α)H), 7.54-7.57 (2H, d, *J* 8.48, C(2'')H and C(6'')H), 7.61-7.63 (4H, m, C(2')H, C(3')H, C(5')H, C(6')H), 7.70 (1H, s, C(2)H), 7.92-7.96 (1H, d, *J* 15.28, C(β)H), 8.31 (1H, s, C(4)H) and 13.16 (1H, s, C(6)OH chelated).

***E*-3-(4-chloro-phenyl)-1-(6-hydroxy-7-methyl-3-phenyl-benzofuran-5-yl)-propenone 14a.** 84 %; orange crystals; mp 198-199 °C; (Found: C, 73.88; H, 4.43. $C_{24}H_{17}O_3Cl$ (388.84) requires C, 74.13; H, 4.40%); υ_{max}/cm^{-1} 3455, 3105,

2966, 1634, 1560, 1522, 1207 and 1167; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.50 (3H, s, C(7)CH_3), 7.44-7.71 (10H, m, C(2')H, C(3')H, C(4')H, C(5')H, C(6')H, C(2'')H, C(3'')H, C(5'')H, C(6'')H, C(α)H), 7.71 (1H, s, C(2)H), 7.90-7.95 (1H, d, *J* 15.52, C(β)H), 8.32 (1H, s, C(4)H) and 12.99(1H, s, C(6)OH chelated).

***E*-3-(4-chloro-phenyl)-1-(6-hydroxy-3-phenyl-benzofuran-5-yl)-propenone 14b.** 81 %; orange crystals; mp 152-153 °C; (Found: C, 73.34; H, 4.01. $C_{23}H_{15}O_3Cl$ (374.82) requires C, 73.70; H, 4.03 %); υ_{max}/cm^{-1} 3439, 3122, 2928, 1633, 1611, 1566, 1528, 1222 and 1151; δ_H (300 MHz; $CDCl_3$; Me_4Si) 7.14 (1H, s, C(7)H), 7.41-7.69 (10H, m, C(2')H, C(3')H, C(4')H, C(5')H, C(6')H, C(2'')H, C(3'')H, C(5'')H, C(6'')H, C(α)H), 7.71 (1H, s, C(2)H), 7.89-7.94 (1H, d, *J* 15.4, C(β)H), 8.29 (1H, s, C(4)H) and 12.98 (1H, s, C(6)OH chelated).

***E*-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-3-phenyl-propenone 22a.** 69 %; orange crystals; mp 190-192 °C; (Found: C, 79.21; H, 5.93. $C_{22}H_{20}O_3$ (332.39) requires C, 79.49; H, 6.06%); υ_{max}/cm^{-1} 3434, 2921, 1638, 1575, 1451, 1404 and 1155; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.82-1.93 (4H, m, C(7)-CH_2- and C(8)-CH_2-), 2.41 (3H, s, C(4)CH_3), 2.65-2.69 (4H, m, C(6)-CH_2- and C(9)-CH_2-), 7.40-7.47 (3H, m, C(3')H, C(4')H and C(5')H), 7.67-7.71 (3H, m, C(α)H, C(2')H and C(6')H), 7.82 (1H, s, C(1)H), 7.84-7.91 (1H, d, *J* 15.49, C(β)H), and 13.12 (1H, s, C(3)OH chelated).

(*E*)-1-(3-Hydroxy-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-3-phenyl-propenone 22b. 77.8 %; orange crystals, mp 178-179 °C; (Found: C, 78.96; H, 5.61. $C_{21}H_{18}O_3$ (318.37) requires C, 79.22; H, 5.69 %); υ_{max}/cm^{-1} 3449, 2931, 1636, 1570, 1460, 1361 and 1145; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.85-1.93 (4H, m, C(7)-CH_2- and C(8)-CH_2-), 2.62-2.69 (4H, m, C(6)-CH_2- and C(9)-CH_2-), 6.98 (1H, s, C(4)-H), 7.43-7.45 (3H, m, C(3')H, C(4')H and C(5')H), 7.67-7.72 (3H, m, C(α)H, C(2')H and C(6')H), 7.87 (1H, s, C(1)H), 7.89-7.95 (1H, d, *J* 15.49, C(β)H) and 13.1 (1H, s, C(3)OH chelated).

***E*-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-3-(4-methoxy-phenyl)-propenone 23a.** 62 %; orange crystals; mp 176-178 °C; (Found: C, 76.11; H 5.97. $C_{23}H_{22}O_4$ (362.42) requires C, 76.22; H, 6.11%); υ_{max}/cm^{-1} 3431, 2939, 1635, 1600, 1564, 1500, 1456, 1388, 1250 and 1139; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.94-1.95 (2H, m, C(8)-CH_2-), 1.95-1.98 (2H, m, C(7)-CH_2-), 2.43 (3H, s, C(4)CH_3), 2.66-2.68 (2H, m, C(9)-CH_2-), 2.71-2.73 (2H, m, C(6)-CH_2-), 3.89 (3H, s, C(4')OCH_3), 6.97-6.98 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.60-7.64 (1H, d, *J* 15.5, C(α)H), 7.65-7.69 (2H, d, *J* 8.8, C(2')H and C(6')H), 7.89 (1H, s, C(1)H), 7.90-7.93 (1H, d, *J* 15.5, C(β)H) and 13.20 (1H, s, C(3)OH chelated).

***E*-1-(3-hydroxy-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-3-(4-methoxy-phenyl)-propenone 23b.** 58 %; orange crystals; mp 159-160 °C; (Found: C, 75.51; H, 5.69. $C_{22}H_{20}O_4$ (348.39) requires C, 75.84; H, 5.78%); υ_{max}/cm^{-1} 3437, 2932, 1637, 1601, 1560, 1509, 1461, 1396, 1257 and 1145; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.91-1.93 (2H, m, C(8)-CH_2-), 1.94-1.97 (2H, m, C(7)-CH_2-), 2.63-2.65 (2H, m, C(9)-CH_2-), 2.69-2.71 (2H, m, C(6)-CH_2-), 3.87 (3H, s, C(4')OCH_3), 6.96-6.98 (2H, d, *J* 8.84, C(3')H and C(5')H), 6.98 (1H, s, C(4)H), 7.58-7.62 (1H, d, *J* 15.5, C(α)H), 7.65-7.68 (2H, d, *J* 8.68, C(2')H and C(6')H), 7.89 (1H, s, C(1)H), 7.89-7.93 (1H, d, *J* 15.5, C(β)H) and 13.19 (1H, s, C(3)OH chelated).

***E*-3-(4-chloro-phenyl)-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-propenone 24a.** 77 %; orange crystals; mp 225-227 °C; (Found: C, 72.31; H, 5.33. $C_{22}H_{19}O_3Cl$ (366.84) requires C, 72.03; H, 5.22%); υ_{max}/cm^{-1} 3429, 2928, 1637, 1611, 1550, 1490, 1451, 1399, 1250 and 1148; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.89-1.95 (2H, m, C(8)-CH_2-), 1.96-1.98 (2H, m, C(7)-CH_2-), 2.40 (3H, s, C(4)CH_3), 2.62-2.65 (2H, m, C(9)-CH_2-), 2.73-2.76 (2H, m, C(6)-CH_2-), 7.42-7.44 (2H, d, *J* 8.6, C(3')H and C(5')H), 7.65-7.63 (2H, d, *J* 8.6, C(2')H and C(6')H), 7.69-7.73 (1H, d, *J* 15.66, C(α)H), 7.74 (1H, s, C(1)H), 7.86-7.90 (1H, d, *J* 15.66, C(β)H) and13.28 (1H, s, C(3)OH chelated).

***E*-3-(4-chloro-phenyl)-1-(3-hydroxy-6,7,8,9-tetrahydro-dibenzofuran-2-yl)-propenone 24b.** 78 %; orange crystals; mp 191-192 °C; (Found: C, 71.61; H, 4.82. $C_{21}H_{17}O_3Cl$ (352.81) requires C, 71.49; H, 4.85%); υ_{max}/cm^{-1} 3448, 2929, 1633, 1621, 1569, 1520, 1468, 1391, 1257 and 1140; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.85-1.89 (2H, m, C(8)-CH_2-), 1.92-1.96 (2H, m, C(7)-CH_2-), 2.62-2.64 (2H, m, C(9)-CH_2-), 2.70-2.72 (2H, m, C(6)-CH_2-), 6.99 (1H, s, C(4)H), 7.41-7.43 (2H, d, *J* 8.4, C(3')H and C(5')H), 7.62-7.64 (2H, d, *J* 8.4, C(2')H and C(6')H), 7.67-7.71 (1H, d, *J* 15.44, C(α)H), 7.86-7.90 (1H, d, *J* 15.36, C(β)H), 7.87 (1H, s, C(1)H) and 13.01 (1H, s, C(3)OH chelated).

General procedure for flavanones (5-7, 15-17, 25-27).

3,9-dimethyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 5a. A mixture of 1-(6-hydroxy-3,7-dimethylbenzofuran-5-yl)-ethanone **1a** (0.0049 moles) and freshly distilled benzaldehyde (0.0049 moles) was refluxed in absolute ethanol (15 cm^3) with catalytic amount of piperidine for 36 h. Reaction was monitored on TLC which showed the formation of chalcone (minor) and flavanone (major). The excess of ethanol was distilled off *in vacuo* and the reaction mixture was then poured into ice-hydrochloric acid and filtered. The product was crystallized from ethanol: toluene mixture to give 3,9-dimethyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **5a** (54 %) as light yellow crystals; mp 153-154 °C; (Found: C, 78.12; H, 5.55. $C_{19}H_{16}O_3$ (292.33) requires C, 78.06; H, 5.51 %); υ_{max}/cm^{-1} 3440, 2936, 1689, 1621, 1474, 1229 and 1130; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.26 (3H, d, *J* 1.1, C(3)CH_3), 2.39 (3H, s, C(9)CH_3), 2.92-2.99 (1H, dd, $J_{vicinal}$ 3.1 and $J_{geminal}$ 16.6, C(6)equatorial H), 3.08-3.19 (1H, dd, $J_{vicinal}$ 12.83 and $J_{geminal}$ 16.4, C(6)axial H), 5.5-5.55 (1H, dd, $J_{vicinal}$ 2.98 and $J_{vicinal}$ 12.8, C(7)axial H), 7.39 (1H, d, *J* 1.1, C(2)H), 7.4-7.59 (5H, m, C(7)phenyl protons) and 8.19 (1H, s, C(4)H).

3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 5b. 49.5 %; light yellow crystals; mp 128-129 °C; (Found: C, 77.59; H, 5.01. $C_{18}H_{14}O_3$ (278.30) requires C, 77.68; H, 5.07 %); υ_{max}/cm^{-1} 3438, 2928, 1677, 1617, 1469, 1233 and 1129; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.24 (3H, d, *J* 0.96, C(3)CH_3), 2.91-2.98 (1H, dd, $J_{vicinal}$ 3.04 and $J_{geminal}$ 16.9, C(6)equatorial H), 3.09-3.19 (1H, dd, $J_{vicinal}$ 12.85 and $J_{geminal}$ 16.9, C(6)axial H), 5.49-5.54 (1H, dd, $J_{vicinal}$ 2.88 and $J_{vicinal}$ 12.85, C(7)axial H), 7.08 (1H, s, C(9)H), 7.36 (1H, d, *J* 0.96, C(2)H), 7.38-7.57 (5H, m, C(7)phenyl protons) and 8.15 (1H, s, C(4)H).

7-(4-methoxy-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 6a. 42.6 %; light yellow crystals; mp 138-139 °C; (Found: C, 74.21; H, 5.34. $C_{20}H_{18}O_4$ (322.35) requires C, 74.51; H, 5.62 %); υ_{max}/cm^{-1} 3116, 2924, 1680, 1624, 1600, 1518, 1477, 1352, 1272, 1251 and 1142; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.24 (3H, d, *J* 1.2, C(3)CH_3), 2.39 (3H, s, C(9)CH_3), 2.92-2.97 (1H, dd, $J_{vicinal}$ 2.8 and $J_{geminal}$ 16.8, C(6)equatorial H), 3.08-3.15 (1H, dd, $J_{vicinal}$ 12.8 and $J_{geminal}$ 16.8, C(6)axial H), 3.86 (3H, s, C(4')OCH_3), 5.44-5.48 (1H, dd, $J_{vicinal}$ 3.2 and $J_{vicinal}$ 12.8, C(7)axial H), 6.97-7.00 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.38 (1H, d, *J* 1.2, C(2)H), 7.45-7.47 (2H, d, *J* 8.8, C(2')H and C(6')H) and 8.01 (1H, s, C(4)H); *m/z* 345.2 (M+23, 16 %), 324.3 (M+2, 26 %) and 323.3 (M+1, 100 %).

7-(4-methoxy-phenyl)-3-methyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 6b. 38 %; light yellow crystals; mp 125-126 °C; (Found: C, 73.71; H, 4.93. $C_{19}H_{16}O_4$ (308.33) requires C, 74.01; H, 5.23%); υ_{max}/cm^{-1} 3440, 2931, 1688, 1621, 1467, 1230 and 1130; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.24 (3H, d, *J* 1.1, C(3)CH_3), 2.87-2.94 (1H, dd, $J_{vicinal}$ 2.86 and $J_{geminal}$ 16.88, C(6)equatorial H), 3.10-3.20 (1H, dd, $J_{vicinal}$ 12.96 and $J_{geminal}$ 16.88, C(6)axial H), 3.84 (3H, s, C(4')OCH_3), 5.43-5.48 (1H, dd, $J_{vicinal}$ 2.7 and $J_{vicinal}$ 12.9, C(7)axial H), 6.95-6.98 (2H, d, *J* 8.68, C(3')H and C(5')H), 7.05 (1H, s, C(9)H), 7.36 (1H, d, *J* 1.1, C(2)H), 7.42-7.45 (2H, d, *J* 8.63, C(2')H and C(6')H) and 8.14(1H, s, C(4)H).

7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 7a. 59 %; light yellow crystals; mp 169-170 °C; (Found: C, 69.57; H, 4.60. $C_{19}H_{15}O_3Cl$ (326.77) requires C, 69.83; H, 4.62%); υ_{max}/cm^{-1} 3126, 2929, 1683, 1629, 1597, 1515, 1471, 1357, 1277, 1255 and 1149; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.2 (3H, d, *J* 1.12, C(3)CH_3), 2.4 (3H, s, C(9)CH_3), 2.93-2.98 (1H, dd, $J_{vicinal}$ 3.2 and $J_{geminal}$ 16.8, C(6)equatorial H), 3.02-3.10 (1H, dd, $J_{vicinal}$ 12.4 and $J_{geminal}$ 16.8, C(6)axial H), 5.48-5.52 (1H, dd, $J_{vicinal}$ 3.2 and $J_{vicinal}$ 12.4, C(7)axial H), 7.40 (1H, d, *J* 1.2, C(2)H), 7.42-7.44 (2H, d, *J* 8.4, C(3')H and C(5')H), 7.47-7.49 (2H, d, *J* 8.4, C(2')H and C(6')H) and 8.02(1H, s, C(4)H); δ_C(100MHz; $CDCl_3$; Me_4Si) 7.87 (C3-*C*H_3), 8.45 (C9-*C*H_3), 44.61 (C-6), 78.76 (C-7), 109.75 (C-9), 115.60 (C-3), 116.58 (C-4a), 117.45 (C-4), 123.79 (C-3a), 127.33 (C-3' and C-5'), 129.00 (C-2' and C-6'), 134.33 (C-4'), 137.81 (C-1'), 142.28 (C-2), 156.92 (C-8a), 158.96 (C-9a) and 192.29 (C5->*C*=O).

7-(4-chloro-phenyl)-3-methyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 7b. 50.5 %; light yellow crystals; mp 136-138 °C; (Found: C, 68.78; H, 3.98. $C_{18}H_{13}O_3Cl$ (312.75) requires C, 69.12; H, 4.18%); υ_{max}/cm^{-1} 3126, 2922, 1689, 1619, 1611, 1520, 1470, 1355, 1271, 1241 and 1144; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.24 (3H, d, *J* 1.11, C(3)CH_3), 2.89-2.96 (1H, dd, $J_{vicinal}$ 3.18 and $J_{geminal}$ 16.88, C(6)equatorial H), 3.03-3.13 (1H, dd, $J_{vicinal}$ 12.58 and $J_{geminal}$ 16.89, C(6)axial H), 5.46-5.51 (1H, dd, $J_{vicinal}$ 3.12 and $J_{vicinal}$ 12.58, C(7)axial H), 7.07 (1H, s, C(9)H), 7.36 (1H, d, *J* 1.11, C(2)H), 7.40-7.43 (2H, d, *J* 8.77, C(3')H and C(5')H), 7.44-7.47 (2H, d, *J* 8.74, C(2')H and C(6')H) and 8.14 (1H, s, C(4)H).

9-methyl-3,7-diphenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 15a. 52.2 %; light yellow crystals; mp 189-190 °C; (Found: C, 81.16; H, 4.81. $C_{24}H_{18}O_3$ (354.40) requires C, 81.33; H, 5.11%); υ_{max}/cm^{-1} 3441, 2937, 1688, 1623, 1471, 1238 and 1132; δ_H (300 MHz; DMSO; Me_4Si) 2.43 (3H, s, C(9)CH_3), 2.92-2.98 (1H, dd, $J_{vicinal}$ 3.1 and $J_{geminal}$ 16.84, C(6)equatorial H), 3.09-3.17 (1H, dd, $J_{vicinal}$ 12.6 and $J_{geminal}$ 16.85, C(6)axial H), 5.51-5.54 (1H, dd, $J_{vicinal}$ 3.1 and $J_{vicinal}$

12.66, C(7)axial H), 7.4-7.84 (11H, m, C(2)H, C(3)phenyl protons, C(7)phenyl protons) and 8.44 (1H, s, C(4)H).

3,7-diphenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 15b. 48 %; light yellow crystals; mp 230-231 °C; (Found: C, 80.52; H, 4.40. $C_{23}H_{16}O_3$ (340.37) requires C, 81.16; H, 4.73%); υ_{max}/cm^{-1} 3439, 2925, 1689, 1620, 1470, 1231 and 1139; δ_H (300 MHz; DMSO; Me_4Si) 2.90-2.97 (1H, dd, $J_{vicinal}$ 3.15 and $J_{geminal}$ 16.88, C(6)equatorial H), 3.07-3.16 (1H, dd, $J_{vicinal}$ 12.56 and $J_{geminal}$ 16.88, C(6)axial H), 5.50-5.54 (1H, dd ,$J_{vicinal}$ 3.07 and $J_{vicinal}$ 12.55, C(7)axial H), 7.18 (1H, s, C(9)H), 7.38-7.82 (11H, m, C(2)H, C(3)phenyl protons, C(7)phenyl protons) and 8.43 (1H, s, C4-H).

7-(4-methoxy-phenyl)-9-methyl-3-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 16a. 41 %; light yellow crystals; mp 211-213 °C; (Found: C, 77.82; H, 5.03. $C_{25}H_{20}O_4$ (384.42) requires C, 78.10; H, 5.24 %); υ_{max}/cm^{-1} 3439, 2928, 1679, 1617, 1465, 1233 and 1131; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.92-2.99 (1H, dd, $J_{vicinal}$ 2.8 and $J_{geminal}$ 16.8, C(6)equatorial H), 3.13-3.23 (1H, dd, $J_{vicinal}$ 12.85 and $J_{geminal}$ 16.82, C(6)axial H), 5.48-5.53 (1H, dd, $J_{vicinal}$ 2.8 and $J_{vicinal}$ 12.8, C(7)axial H), 6.96-6.99 (2H, d, *J* 8.62, C(3')H and C(5')H), 7.40-7.75 (8H, m, C(2)H, C(3)phenyl protons, C(2')H, C(6')H) and 8.49(1H, s, C(4)H).

7-(4-methoxy-phenyl)-3-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 16b. 39.8 %; light yellow crystals; mp 162-163 °C; (Found: C, 77.98; H, 4.91. $C_{24}H_{18}O_4$ (370.40) requires C, 77.82; H, 4.89 %); υ_{max}/cm^{-1} 3440, 2930, 1682, 1623, 1469, 1232 and 1131; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.90-2.97 (1H, dd, $J_{vicinal}$ 2.9 and $J_{geminal}$ 16.88, C(6)equatorial H), 3.12-3.22 (1H, dd, $J_{vicinal}$ 12.87 and $J_{geminal}$ 16.88, C(6)axial H), 5.46-5.51 (1H, dd, $J_{vicinal}$ 2.7 and $J_{vicinal}$ 12.83, C(7)axial H), 6.96-6.99 (2H, d, *J* 8.66, C(3')H and C(5')H), 7.16 (1H, s, C(9)H), 7.37-7.75 (8H, m, C(2)H, C(3)phenyl protons, C(2')H, C(6')H) and 8.45 (1H, s, C(4)H).

7-(4-chloro-phenyl)-9-methyl-3-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 17a. 59.7 %; light yellow crystals; mp 202-203 °C; (Found: C, 73.88; H, 4.43. $C_{24}H_{17}O_3Cl$ (388.84) requires C, 74.13; H, 4.40 %); υ_{max}/cm^{-1} 3441, 2930, 1688, 1622, 1471, 1233 and 1129; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.46 (3H, s, C(9)CH_3), 2.95-3.00 (1H, dd, $J_{vicinal}$ 3.6 and $J_{geminal}$ 16.8, C(6)equatorial H), 3.04-3.11 (1H, dd, $J_{vicinal}$ 12.4 and $J_{geminal}$ 16.8, C(6)axial H), 5.50-5.54 (1H, dd, $J_{vicinal}$ 3.2 and $J_{vicinal}$ 12.4, C(7)axial H), 7.39-7.52 (7H, m, C(3)phenyl protons, C(3')H, C(5')H), 7.65-7.67 (2H, d, *J* 8.4, C(2')H and C(6')H), 7.79 (1H, s, C(2)H) and 8.32 (1H, s, C(4)H).

7-(4-chloro-phenyl)-3-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 17b. 61 %; light yellow crystals; mp 186-187 °C; (Found: C, 73.34; H, 4.01. $C_{23}H_{15}O_3Cl$ (374.82) requires C, 73.70; H, 4.03 %); υ_{max}/cm^{-1} 3448, 2931, 1682, 1629, 1471, 1229 and 1130; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.92-2.98 (1H, dd, $J_{vicinal}$ 3.15 and $J_{geminal}$ 16.88, C(6)equatorial H), 3.06-3.16 (1H, dd, $J_{vicinal}$ 12.56 and $J_{geminal}$ 16.88, C(6)axial H), 5.50-5.55 (1H, dd, $J_{vicinal}$ 3.07 and $J_{vicinal}$ 12.55, C(7)axial H), 7.18 (1H, s, C(9)H), 7.38-7.76 (10H, m, C(2)H, C(3)phenyl protons, C(7)phenyl protons) and 8.45(1H, s, C(4)H).

10-methyl-8-phenyl-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one 25a. 49 %; light yellow crystals; mp 172-174 °C; (Found: C, 79.21; H, 5.93. $C_{22}H_{20}O_3$ (332.39) requires C, 79.49; H, 6.06 %); υ_{max}/cm^{-1} 3441, 2938, 1681, 1622, 1479, 1236 and 1135; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.85-1.87 (2H, m, C(3)-CH_2-), 1.94-1.96 (2H, m, C(2)-CH_2-), 2.41 (3H, s, C(10)CH_3), 2.59-2.62 (2H, m, C(4)-CH_2-), 2.72-2.75 (2H, m, C(1)-CH_2-), 2.93-2.98 (1H, dd, $J_{vicinal}$ 3.2 and $J_{geminal}$ 16.8, C(7)equatorial H), 3.05-3.13 (1H, dd, $J_{vicinal}$ 12.8 and $J_{geminal}$ 16.8, C(7)axial H), 5.49-5.53 (1H, dd, $J_{vicinal}$ 2.8 and $J_{vicinal}$ 12.8, C(8)axial H), 738-7.42 (1H, m, C(4')H), 7.44-7.48 (2H, m, C(3')H and C(5')H), 7.53-7.56 (2H, m, C(2')H and C(6')H) and 7.88 (1H, s, C(5)H).

8-Phenyl-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one 25b. 52 %; light yellow crystals, mp 97-98 °C; (Found: C, 78.96; H, 5.61. $C_{21}H_{18}O_3$ (318.37) requires C, 79.22; H, 5.69 %); υ_{max}/cm^{-1} 3448, 2932, 1684, 1627, 1475, 1239 and 1135; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.82-1.90 (2H, m, C(3)-CH_2-), 1.91-1.94 (2H, m, C(2)-CH_2-), 2.59-2.61 (2H, m, C(4)-CH_2-), 2.68-2.70 (2H, m, C(1)-CH_2-), 2.89-2.94 (1H, dd, $J_{vicinal}$ 2.6 and $J_{geminal}$ 16.8, C(7)equatorial H), 3.08-3.15 (1H, dd, $J_{vicinal}$ 12.9 and $J_{geminal}$ 16.8, C(7)axial H), 5.47-5.51 (1H, dd, $J_{vicinal}$ 2.6 and $J_{vicinal}$ 12.9, C(8)axial H), 7.02 (1H, s, C(10)H), 7.36-7.51 (5H, m, C(8)phenyl protons) and 7.99 (1H, s, C(5)H).

8-(4-methoxy-phenyl)-10-methyl-1,2,3,4,7,8-hexahydro-9,11-dioxa benzo[*b*]fluoren-6-one 26a. 47 %; light yellow crystals; mp 187-189 °C; (Found: C, 76.11; H, 5.97. $C_{23}H_{22}O_4$ (362.42) requires C, 76.22; H, 6.11 %); υ_{max}/cm^{-1} 3441, 2936, 1688, 1622, 1471, 1233 and 1129; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.85-1.92 (2H, m, C(3)-CH_2-), 1.92-1.95 (2H, m, C(2)-CH_2-), 2.4 (3H, s, C(10)CH_3), 2.59-2.62 (2H, m, C(4)-CH_2-), 2.69-2.72 (2H, m, C(1)-CH_2-), 2.92-2.96 (1H, dd, $J_{vicinal}$ 2.7 and $J_{geminal}$ 16.7, C(7)equatorial H), 3.10-3.19 (1H, dd, $J_{vicinal}$ 13.2 and $J_{geminal}$ 16.8, C(7)axial H), 3.88 (3H, s, C(4')OCH_3), 5.50-5.55 (1H, dd, $J_{vicinal}$ 2.62 and $J_{vicinal}$ 12.98, C(8)axial H), 6.98-7.00 (2H, d, *J* 8.6, C(3')H and C(5')H), 7.68-7.10 (2H, d, *J* 8.6, C(2')H and C(6')H) and 8.05 (1H, s, C(5)H).

8-(4-methoxy-phenyl)-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one 26b. 44.8 %; light yellow crystals; mp 115-117 °C; (Found: C, 75.51; H, 5.69. $C_{22}H_{20}O_4$ (348.39) requires C, 75.84; H, 5.78 %); υ_{max}/cm^{-1} 3448, 2933, 1684, 1621, 1465, 1240 and 1131; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.83-1.91 (2H, m, C(3)-CH_2-), 1.92-1.94 (2H, m, C(2)-CH_2-), 2.58-2.61 (2H, m, C(4)-CH_2-), 2.69-2.70 (2H, m, C(1)-CH_2-), 2.90-2.94 (1H, dd, $J_{vicinal}$ 2.6 and $J_{geminal}$ 16.8, C(7)equatorial H), 3.08-3.17 (1H, dd, $J_{vicinal}$ 13.16 and $J_{geminal}$ 16.8, C(7)axial H), 3.88 (3H, s, C(4')OCH_3), 5.48-5.53 (1H, dd, $J_{vicinal}$ 2.46 and $J_{vicinal}$ 12.96,

C(8)axial H), 6.97-6.99 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.06 (1H, s, C(10)H), 7.67-7.69 (2H, d, *J* 8.8, C(2')H and C(6')H) and 8.00 (1H, s, C(5)H).

8-(4-chloro-phenyl)-10-methyl-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one 27a. 41 %; light yellow crystals; mp 201-203 °C; (Found: C, 72.31; H, 5.33. $C_{22}H_{19}O_3Cl$ (366.84) requires C, 72.03; H, 5.22 %); υ_{max}/cm^{-1} 3441, 2931, 1689, 1624, 1470, 1233 and 1138; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.84-1.89 (2H, m, C(3)-CH_2-), 1.92-1.96 (2H, m, C(2)-CH_2-), 2.4 (3H, s, C(10)CH_3), 2.60-2.61 (2H, m, C(4)-CH_2-), 2.69-2.72 (2H, m, C(1)-CH_2-), 2.88-2.93 (1H, dd, $J_{vicinal}$ 2.93 and $J_{geminal}$ 16.86, C(7)equatorial H), 3.05-3.13 (1H, dd, $J_{vicinal}$ 12.9 and $J_{geminal}$ 16.86, C(7)axial H), 5.46-5.50 (1H, dd, $J_{vicinal}$ 2.9 and $J_{vicinal}$ 12.8, C(8)axial H), 7.39-7.41 (2H, d, *J* 8.52, C(3')H and C(5')H), 7.46-7.48 (2H, d, *J* 8.52, C(2')H and C(6')H) and 7.99 (1H, s, C(5)H).

8-(4-chloro-phenyl)-1,2,3,4,7,8-hexahydro-9,11-dioxa-benzo[*b*]fluoren-6-one 27b. 55 %; light yellow crystals; mp 177-178 °C; (Found: C, 71.61; H, 4.82. $C_{21}H_{17}O_3Cl$ (352.81) requires C, 71.49; H, 4.85 %); υ_{max}/cm^{-1} 3441, 2929, 1679, 1621, 1470, 1233 and 1139; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.82-1.87 (2H, m, C(3)-CH_2-), 1.92-1.96 (2H, m, C(2)-CH_2-), 2.59-2.61 (2H, m, C(4)-CH_2-), 2.68-2.71 (2H, m, C(1)-CH_2-), 2.87-2.92 (1H, dd, $J_{vicinal}$ 2.9 and $J_{geminal}$ 16.8, C(7)equatorial H), 3.02-3.10 (1H, dd, $J_{vicinal}$ 12.9 and $J_{geminal}$ 16.8, C(7)axial H), 5.45-5.49 (1H, dd, $J_{vicinal}$ 2.7 and $J_{vicinal}$ 12.8, C(8)axial H), 7.01 (1H, s, C(10)H), 7.39-7.41 (2H, d, *J* 8.48, C(3')H and C(5')H), 7.43-7.45 (2H, d, *J* 8.48, C(2')H and C(6')H) and 7.98 (1H, s, C(5)H).

General procedure for flavones (8-10, 18-20, 28-30).

3,9-dimethyl-7-phenyl-furo[3,2-*g*]chromen-5-one 8a. A mixture of 3,9-dimethyl-7-phenyl-6,7-dihydro-furo[3,2-g]chromen-5-one **5a** (0.0034 moles) and DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) (0.0051 moles) was refluxed in dry toluene (15 cm^3) for 12 h. The reaction mixture was washed with water

followed by washing with 10 % potassium carbonate solution and then again with water. The toluene layer was dried over sodium sulfate and solvent was distilled off *in vacuo*. The product was purified by column chromatography using petroleum ether (60-80 °C): ethyl acetate mixture (7:3) as eluent to give 3,9-dimethyl-7-phenyl-furo[3,2-*g*]chromen-5-one **8a** (91 %) as light brown crystals; mp 180 °C dec; (Found: C, 78.44; H, 4.69. $C_{19}H_{14}O_3$ (290.31) requires C, 78.60; H, 4.86 %); υ_{max}/cm^{-1} 2933, 1655, 1622, 1617, 1519, 1479, 1361, 1263, 1128 and 821; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.33 (3H, d, *J* 0.6, C(3)CH_3), 2.74 (3H, s, C(9)CH_3), 6.83 (1H, s, C(6)H), 7.50 (1H, d, *J* 0.6, C(2)H), 7.52-8.01 (5H, m, C(7)phenyl protons) and 8.44 (1H, s, C(4)H).

Mole ratio of DDQ used for compounds **(28-30)** was 3.5 equivalents.

3-methyl-7-phenyl-furo[3,2-*g*]chromen-5-one 8b. 86.6 %; light brown crystals; mp 194 °C dec; (Found: C, 78.58; H, 4.61. $C_{18}H_{12}O_3$ (276.28) requires C, 78.25; H, 4.37 %); υ_{max}/cm^{-1} 2918, 1648, 1636, 1619, 1525, 1479, 1358, 1260 and 1133; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.30 (3H, d, *J* 0.58, C(3)CH_3), 6.8 (1H, s, C(6)H), 7.44-8.00 (7H, m, C(2)H, C(9)H, C(7)phenyl protons) and 8.43 (1H, s, C(4)H).

7-(4-methoxy-phenyl)-3,9-dimethyl-furo[3,2-*g*]chromen-5-one 9a. 67.6 %; light brown crystals; mp 248 °C dec; (Found: C, 75.24; H, 5.37. $C_{20}H_{16}O_4$ (320.34) requires C, 74.98; H, 5.03 %); υ_{max}/cm^{-1} 2921, 1657, 1621, 1610, 1507, 1477, 1361, 1254 and 1133; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.29 (3H, d, *J* 1.2, C(3)CH_3), 2.72 (3H, s, C(9)CH_3), 3.91 (3H, s, C(4')OCH_3), 6.82 (1H, s, C(6)H), 7.04-7.06 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.51 (1H, d, *J* 1.2, C(2)H), 7.92-7.94 (2H, d, *J* 8.8, C(2')H and C(6')H) and 8.25(1H, s, C(4)H); δ_C (100MHz; $CDCl_3$; Me_4Si) 7.92 (C3-*C*H_3), 8.75 (C9-*C*H_3), 55.53 (C4'-O*C*H_3), 104.49 (C-6), 109.79 (C-9), 113.32 (C-3' and C-5'), 114.52 (C-3), 116.58 (C-4a), 119.71 (C-4), 124.35 (C-3a), 126.88 (C-2' and C-6'), 127.95 (C-1'), 143.41 (C-2), 152.10 (C-8a), 156.80 (C-4'), 162.39 (C-9a), 163.32 (C-7) and 179.33 (C5->*C*=O).

7-(4-methoxy-phenyl)-3-methyl-furo[3,2-*g*]chromen-5-one 9b. 69.8 %; light brown crystals; mp 238-240 °C dec; (Found: C, 74.62; H, 4.69. $C_{19}H_{14}O_4$ (306.31) requires C, 74.50; H, 4.60 %); υ_{max}/cm^{-1} 2935, 1647, 1636, 1612, 1518, 1477, 1361, 1259, 1127 and 831; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.32 (3H, d, *J* 0.58, C(3)CH_3), 3.91 (3H, s, C(4')OCH_3), 6.76 (1H, s, C(6)H), 7.03-7.06 (2H, d, *J* 8.88, C(3')H and C(5')H), 7.51 (1H, d, *J* 0.58, C(2)H), 7.60 (1H, s, C(9)H), 7.90-7.93 (2H, d, *J* 8.88, C(2')H and C(6')H) and 8.41(1H, s, C(4)H).

7-(4-chloro-phenyl)-3,9-dimethyl-furo[3,2-*g*]chromen-5-one 10a. 88 %; light brown crystals; mp 210 °C dec; (Found: C, 70.21; H, 4.01. $C_{19}H_{13}O_3Cl$ (324.76) requires C, 70.26; H, 4.03 %); υ_{max}/cm^{-1} 2933, 1656, 1621, 1615, 1515, 1472, 1360, 1263, 1129 and 821; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.30 (3H, d, *J* 0.58, C(3)CH_3), 2.73 (3H, s, C(9)CH_3), 6.87 (1H, s, C(6)H), 7.42-7.44 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.50 (1H, d, *J* 0.58, C(2)H), 7.56-7.58 (2H, d, *J* 8.8, C(2')H and C(6')H) and 8.50 (1H, s, C(4)H).

7-(4-chloro-phenyl)-3-methyl-furo[3,2-*g*]chromen-5-one 10b. 86 %; light brown crystals; mp 250-252 °C dec; (Found: C, 69.33; H, 3.40. $C_{18}H_{11}O_3Cl$ (310.73) requires C, 69.57; H, 3.56 %); υ_{max}/cm^{-1} 2920, 1661, 1623, 1601, 1519, 1478, 1359, 1262, 1133 and 838; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.30 (3H, d, *J* 0.58, C(3)CH_3), 6.85 (1H, s, C(6)H), 7.42-7.44 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.45-7.95 (4H, m, C(2)H, C(9)H, C(2')H, C(6')H) and 8.48 (1H, s, C(4)H).

9-methyl-3,7-diphenyl-furo[3,2-*g*]chromen-5-one 18a. 76 %; light brown crystals; mp 220-222 °C dec; (Found: C, 81.84; H, 4.61. $C_{24}H_{16}O_3$ (352.38) requires C, 81.80; H, 4.57 %); υ_{max}/cm^{-1} 2919, 1648, 1621, 1611, 1525, 1479, 1359, 1262 and 1133; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.80 (3H, s, C(9)CH_3), 6.94 (1H, s, C(6)H), 7.41-8.1 (11H, m, C(2)H, C(7)phenyl protons, C(3)phenyl protons) and 8.77 (1H, s, C(4)H).

3,7-diphenyl-furo[3,2-*g*]chromen-5-one 18b. 71 %; light brown crystals; mp 200 °C dec; (Found: C, 81.49; H, 4.05. $C_{23}H_{14}O_3$ (338.36) requires C, 81.64; H, 4.17 %); υ_{max}/cm^{-1} 2933, 1658, 1622, 1599, 1511, 1471, 1359, 1260, 1131 and 833; δ_H (400 MHz; $CDCl_3$; Me_4Si) 6.92 (1H, s, C(6)H), 7.43-8.01 (12H, m, C(2)H, C(9)H, C(7)phenyl protons, C(3)phenyl protons) and 8.75 (1H, s, C(4)H); *m/z* 361.1 (M+23, 11%), 340.1 (M+2, 22) and 339.1 (M+1, 100).

7-(4-methoxy-phenyl)-9-methyl-3-phenyl-furo[3,2-*g*]chromen-5-one 19a. 79 %; light brown crystals; mp 200 °C dec; (Found: C, 78.51; H, 4.70. $C_{25}H_{18}O_4$ (382.41) requires C, 78.52; H, 4.74 %); υ_{max}/cm^{-1} 2933, 1651, 1626, 1602, 1515, 1480, 1359, 1261, 1133 and 819; δ_H (400 MHz; DMSO; Me_4Si) 2.70 (3H, s, C(9)CH_3), 3.93 (3H, s, C(4')OCH_3), 6.90 (1H, s, C(6)H), 7.05-7.07 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.40-8.05 (8H, m, C(2)H, C(2')H, C(6')H, C(3)phenyl protons) and 8.75 (1H, s, C(4)-H).

7-(4-methoxy-phenyl)-3-phenyl-furo[3,2-*g*]chromen-5-one 19b. 80 %; light brown crystals; mp 258 °C dec; (Found: C, 78.49; H, 4.65. $C_{24}H_{16}O_4$ (368.38) requires C, 78.25; H, 4.37 %); υ_{max}/cm^{-1} 2919, 1642, 1616, 1612, 1525, 1477, 1361, 1262, 1133 and 836; δ_H (400 MHz; DMSO; Me_4Si) 3.92 (3H, s, C(4')OCH_3), 6.91 (1H, s, C(6)H), 7.04-7.06 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.43-8.01 (9H, m, C(2)H, C(9)H, C(2')H, C(6')H, C(3)phenyl protons) and 8.73 (1H, s, C(4)H).

7-(4-chloro-phenyl)-9-methyl-3-phenyl-furo[3,2-*g*]chromen-5-one 20a. 83.2 %; light brown crystals; mp 230 °C dec; (Found: C, 74.31; H, 3.81. $C_{24}H_{15}O_3Cl$ (386.83) requires C, 74.51; H, 3.90 %); υ_{max}/cm^{-1} 2936, 1656, 1622, 1611, 1519, 1477, 1361, 1260, 1135 and 836; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.80 (3H, s, C(9)CH_3), 6.90 (1H, s, C(6)H), 7.42-7.95 (10H, m, C(2)H, C(7)phenyl protons, C(3)phenyl protons) and 8.59 (1H, s, C(4)H).

7-(4-chloro-phenyl)-3-phenyl-furo[3,2-*g*]chromen-5-one 20b. 89 %; light brown crystals; mp 210 °C dec; (Found: C, 73.87; H, 3.39. $C_{23}H_{13}O_3Cl$ (372.80) requires C, 74.10; H, 3.51 %); υ_{max}/cm^{-1} 2929, 1646, 1622, 1588, 1525, 1476, 1361, 1260, 1131 and 834; δ_H (400 MHz; $CDCl_3$; Me_4Si) 6.88 (1H, s, C(6)H), 7.4-8.00 (11H, m, C(2)H, C(9)H, C(7)phenyl protons, C(3)phenyl protons) and 8.56 (1H, s, C(4)H).

10-methyl-8-phenyl-9,11-dioxa-benzo[*b*]fluoren-6-one 28a. 81 %; light brown crystals; mp 264 °C dec; (Found: C, 80.79; H, 4.07. $C_{22}H_{14}O_3$ (326.34) requires C, 80.96; H, 4.32%); υ_{max}/cm^{-1} 2922, 1649, 1622, 1600, 1511, 1488, 1360, 1259, 1133 and 819; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.82 (3H, s, C(10)CH_3), 6.96 (1H, s, C(7)H), 7.38-8.01 (9H, m, C(8)phenyl protons, C(1)H, C(2)H, C(3)H, C(4)H) and 8.66 (1H, s, C(5)H).

8-Phenyl-9,11-dioxa-benzo[*b*]fluoren-6-one 28b. 79 %; light brown crystals, mp 200 °C dec; (Found: C, 80.49; H, 3.82. $C_{21}H_{12}O_3$ (312.32) requires C, 80.75; H, 3.87 %); υ_{max}/cm^{-1} 2923, 1650, 1626, 1609, 1515, 1481, 1364, 1269, 1137 and 826; δ_H (300 MHz; DMSO; Me_4Si) 7.06 (1H, s, C(7)H), 7.36-8.36 (10H, m, C(8)phenyl protons, C(1)H, C(2)H, C(3)H, C(4)H, C(10)H) and 8.85 (1H, s, C(5)H).

8-(4-methoxy-phenyl)-10-methyl-9,11-dioxa-benzo[*b*]fluoren-6-one 29a. 74 %; light brown crystals; mp 230 °C dec; (Found: C, 77.28; H, 4.33. $C_{23}H_{16}O_4$ (356.37) requires C, 77.51; H, 4.52 %); υ_{max}/cm^{-1} 2919, 1645, 1622, 1599, 1520, 1477, 1359, 1271, 1133 and 828; δ_H (300 MHz; DMSO; Me_4Si) 2.43 (3H, s, C(10)CH_3), 3.93 (3H, s, C(4')OCH_3), 6.97-6.99 (2H, d, *J* 8.5, C(3')H and C(5')H), 7.10 (1H, s, C(7)H), 7.43-7.98 (6H, m, C(2')H, C(6')H, C(1)H, C(2)H, C(3)H, C(4)H) and 8.84(1H, s, C(5)H).

8-(4-methoxy-phenyl)-9,11-dioxa-benzo[*b*]fluoren-6-one 29b. 77.8 %; light brown crystals; mp 256 °C dec; (Found: C, 77.05; H, 3.93. $C_{22}H_{14}O_4$ (342.34)

requires C, 77.18; H, 4.12 %); υ_{max}/cm^{-1} 2919, 1658, 1619, 1611, 1519, 1488, 1366, 1261, 1133 and 822; δ_H (300 MHz; DMSO; Me_4Si) 3.90 (3H, s, C(4')OCH_3), 6.96-6.98 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.08 (1H, s, C(7)H), 7.4-8.4 (7H, m, C(2')H, C(6')H, C(1)H, C(2)H, C(3)H, C(4)H, C(10)H) and 8.83 (1H, s, C(5)H).

8-(4-chloro-phenyl)-10-methyl-9,11-dioxa-benzo[*b*]fluoren-6-one 30a. 79.5 %; light brown crystals; mp 215 °C dec; (Found: C, 73.08; H, 3.49. $C_{22}H_{13}O_3Cl$ (360.79) requires C, 73.23; H, 3.63 %); υ_{max}/cm^{-1} 2929, 1647, 1621, 1597, 1525, 1477, 1358, 1260 and 1133; δ_H (300 MHz; DMSO; Me_4Si) 2.44 (3H, s, C(10)CH_3), 7.11 (1H, s, C(7)H), 7.41-7.43 (2H, d, *J* 8.8, C(3')H and C(5')H), 7.45-7.47 (2H, d, *J* 8.8, C(2')H and C(6')H), 7.45-8.00 (4H, m, C(1)H, C(2)H, C(3)H, C(4)H) and 8.83 (1H, s, C(5)H).

8-(4-chloro-phenyl)-9,11-dioxa-benzo[*b*]fluoren-6-one 30b. 88 %; light brown crystals; mp 278 °C dec; (Found: C, 72.98; H, 3.41. $C_{21}H_{11}O_3Cl$ (346.76) requires C, 72.73; H, 3.19 %); υ_{max}/cm^{-1} 2919, 1655, 1622, 1600, 1525, 1489, 1361, 1260, 1131 and 820; δ_H (300 MHz; DMSO; Me_4Si) 7.10 (1H, s, C(7)H), 7.40-7.42 (2H, d, *J* 8.4, C(3')H and C(5')H), 7.44-7.46 (2H, d, *J* 8.4, C(2')H and C(6')H), 7.45-8.20 (5H, m, C(1)H, C(2)H, C(3)H, C(4)H, C(10)H) and 8.82 (1H, s, C(5)H).

***E*-6-benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 31.** It was isolated when molar excess (1:2.5) of aldehyde was used. Yellow crystals; mp 212-214 °C; (Found: C, 81.76; H, 4.83. $C_{25}H_{18}O_3$ (366.41) requires C, 81.94; H, 4.95 %); υ_{max}/cm^{-1} 3099, 1670, 1621, 1481, 1477 and 1129; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.17 (3H, d, *J* 1.5, C(3)CH_3), 6.66 (1H, s, C(7)H), 6.96 (1H, s, C(9)H), 7.25-7.51 (11H, m, C(2)H, C(7)phenyl protons, C(2')H, C(3')H, C(4')H, C(5')H, C(6')H), 8.12 (1H, s, vinylic proton) and 8.15 (1H, s, C(4)H).

***E*-6-(4-chloro-benzylidene)-7-(4-chloro-phenyl)-3-methyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 32.** Yellow crystals; mp 189-190 °C; (Found: C,

69.01; H, 3.84. $C_{25}H_{16}O_3Cl_2$ (435.30) requires C, 68.98; H, 3.70 %); υ_{max}/cm^{-1} 3095, 1672, 1624, 1488, 1471 and 1132; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.18 (3H, d, *J* 0.9, C(3)CH_3), 6.53 (1H, s, C(7)H), 6.95 (1H, s, C(9)H), 7.19-7.42 (9H, m, C(2)H, C(7)phenyl protons, C(2')H, C(3')H, C(5')H, C(6')H), 8.09 (1H, s, vinylic proton) and 8.12 (1H, s, C(4)H).

***E*-6-(4-methoxy-benzylidene)-7-(4-methoxy-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 33.** Yellow crystals; mp 150-152 °C; (Found: C, 76.21; H, 5.37. $C_{28}H_{24}O_5$ (440.49) requires C, 76.34; H, 5.49 %); υ_{max}/cm^{-1} 3119, 2999, 1669, 1628, 1600, 1519, 1472, 1249, 1188 and 1120; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.18 (3H, d, *J* 0.9, C(3)CH_3), 2.36 (3H, s, C(9)CH_3), 3.74 (3H, s, C(4")OCH_3), 3.83 (3H, s, C(4')OCH_3), 6.69 (1H, s, C(7)H), 6.81-6.84 (2H, d, *J* 8.64, C(3")H and C(5")H), 6.88-6.91 (2H, d, *J* 8.64, C(3')H and C(5')H), 7.25-7.29 (3H, m, C(2)H, C(2")H, C(6")H), 7.41-7.44 (2H, d, *J* 8.57, C(2')H and C(6')H), 8.00 (1H, s, vinylic proton) and 8.10 (1H, s, C(4)H).

***E*-6-(4-methoxy-benzylidene)-7-(4-methoxy-phenyl)-9-methyl-3-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 34.** Yellow crystals; mp 164-166 °C; (Found: C, 78.97; H, 5.52. $C_{33}H_{26}O_5$ (502.56) requires C, 78.86; H, 5.21 %); υ_{max}/cm^{-1} 3123, 2993, 1671, 1621, 1602, 1509, 1477, 1251, 1181 and 1115; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.38 (3H, s, C(9)CH_3), 3.75 (3H, s, C(4")OCH_3), 3.83 (3H, s, C(4')OCH_3), 6.70 (1H, s, C(7)H), 6.82-6.84 (2H, d, *J* 8.6, C(3")H and C(5")H), 6.88-6.90 (2H, d, *J* 8.64, C(3')H and C(5')H), 7.26-7.29 (2H, d, *J* 8.6Hz, C(2")H and C(6")H), 7.40-7.92 (8H, m, C(2)H, C(2')H, C(6')H, C(3)phenyl protons), 8.01 (1H, s, vinylic proton) and 8.13 (1H, s, C(4)H).

Photo chemical isomerization of *E*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 31 to *Z*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 35. *E*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **31** (0.005 moles) was dissolved in toluene (15 cm^3) and kept in a chamber containing 150W mercury arc lamp for 12

h. Excess of toluene was distilled off *in vacuo* and the product was purified by column chromatography on neutral alumina using petroleum ether (60-80 °C): ethyl acetate mixture (8:2) as eluent. Use of silica gel was showing some conversion of *Z* isomer back into the *E* isomer. *Z*-6-Benzylidene-3-methyl-7-phenyl-6,7-dihydro-furo[3,2-g]chromen-5-one **35** (81.2 %) was obtained as yellow crystals, mp 101-103 °C; (Found: C, 81.76; H, 4.83. $C_{25}H_{18}O_3$ (366.41) requires C, 81.94; H, 4.95 %); υ_{max}/cm^{-1} 3069, 2942, 1661, 1624, 1583, 1468, 1453, 1224, 1182, 1128 and 737; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.25 (3H, d, *J* 1.5, C(3)CH_3), 6.15 (1H, s, C(7)H), 6.77 (1H, s, vinylic proton), 7.09 (1H, s, C(9)H), 7.26-7.70 (11H, m, C(2)H, C(7)phenyl protons, C(2')H, C(3')H, C(4')H, C(5')H, C(6')H) and 8.12 (1H, s, C(4)H).

3.A.4 Conclusions

- Present investigation provides a one-pot process for the synthesis of furoflavanones. The reaction when carried out in sodium hydroxide gave chalcone as the exclusive product, while reaction in piperidine gave flavanone as the major product along with chalcone (minor).

- NMR of furoflavanone is a typical ABX system, which shows the existence of flavanone ring in a quasi chair conformation with phenyl ring equatorial.

- Molar excess of aryl aldehyde in the preparation of flavanones using piperidine, leads to the formation of 3-arylidene flavanones as a co-product in *E*-configuration as confirmed from ^{1}H-NMR.

- One of the chalcone synthesized, *E*-3-(4-chloro-phenyl)-1-(3-hydroxy-4-methyl-6,7,8,9-tetrahydro-dibenzofuran-2-yl) propenone **24a** shows better anti-inflammatory activity than standard drug Ibuprofen. One of the flavone, 3,7-diphenyl-furo[3,2-*g*]chromen-5-one **18b**, shows growth inhibition upto 74 % against Breast MCF–7 cancer cell line and 40 % against Prostate DU-145 cell line. These results show the need to explore other compounds for possible anti-inflammatory and anti-cancer activity.

3.A.5 References

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Chapter 3: Section B

CONFORMATION OF FUROFLAVANONES

3.B.1 Introduction

Conformations of a molecule are defined as the various arrangements of its atoms in space which differ only in rotation around single bond or bonds (i.e., in dihedral angles) and are easily interconvertible. Riddell (1980) proposed that conformations are stereoisomers that can be interconverted either by rotations around bonds of order approximately one with any concomitant small distortion at bond lengths and angles or by inversion at a three coordinate centre in the molecule or by pseudorotation on phosphorus.

Quasi chair conformation in flavanones

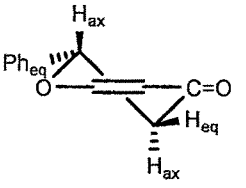
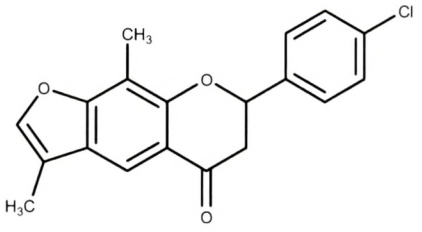


Figure 1: Quasi chair conformation.

- The said conformation **(Figure 1)** was proposed by Philbin and wheeler.[1]
- [illegible] are explained.
- However, no reports have been found hitherto for the conformation of furoflavanones by X-ray crystallography.

3.B.2 Results and Discussion



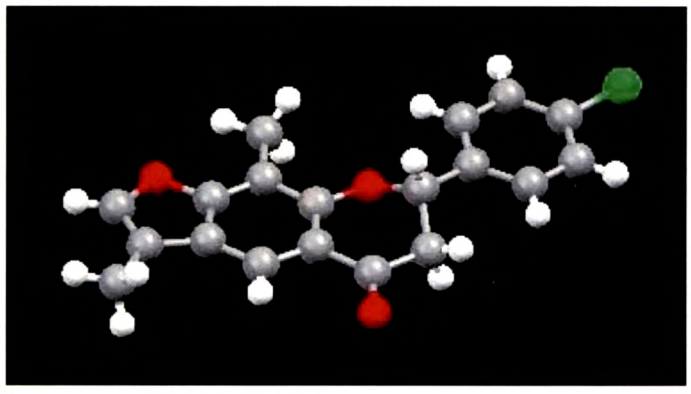


Figure 2: Crystal structure of 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **7a**.

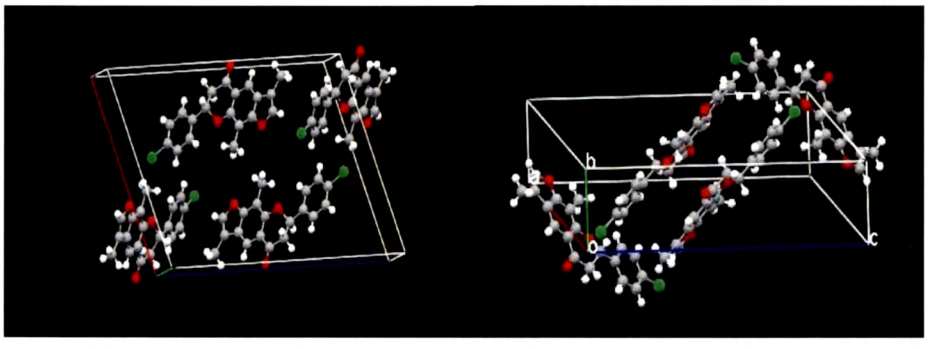


Figure 3: Packing structure in 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **7a**.

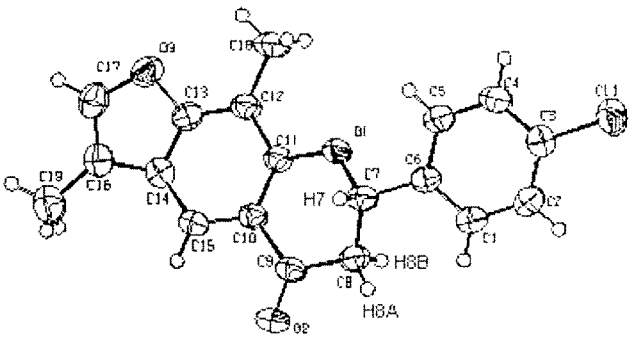


Figure 4: ORTEP diagram of 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one **7a** (50% probability factor for thermal ellipsoid with atom numbering scheme).

Crystal structure of furoflavanone: 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 7a.

Compound crystallizes in a centro symmetric monoclinic space group $P2_1/c$. **Figure 2** shows the crystal structure of 7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-g]chromen-5-one **7a** whereas, the packing structure can be seen in **Figure 3,** generated using Mercury 1.4.2 software.[2] The asymmetric unit consists of a single flavanone molecule at a normal position. As can be seen from **Figure 4** (ORTEP diagram), flavanone ring exists in quasi-chair conformation, with phenyl ring at equatorial position. The crystal structure shows the (*S*)-configuration of furoflavanone. All the atoms apart from C-7 are coplanar. Atom C-7 deviates from the plane defined by atoms C8/C9/C10/C11/O1 by 0.610 Å. The dihedral angle between the planes formed by O1/C7/C8 and C8/C9/C10/C11/O1 is 47.20° whereas the dihedral angle between C1/C2/C3/C4/C5/C6 and C8/C9/C10/C11/O1 planes is 4.56°. The torsion angle –54.31 for H7-C7-C8-$H8_A$ indicates that H-7 and $H8_A$ are not in one plane i.e. H-7 is axial and H-8_A is equatorial, while the torsion angle –171.97 for H7-C7-C8-$H8_B$ indicates that H-7 and H-8_B are almost in one plane i.e. H-7 is axial and H-8_B

is also axial. The torsion angle –51.16 for C6-C7-C8-$H8_B$ indicates that phenyl ring and $H\text{-}8_B$ are not in one plane (i.e. phenyl ring is equatorial and $H\text{-}8_B$ is axial). Further, the torsion angle –81.77 for H7-C7-C6-C5 and 95.76 for H7-C7-C6-C1 clearly indicates that phenyl ring and H-7 are almost perpendicular to each other i.e. H-7 is axial and phenyl ring is equatorial and parallel to the plane formed by C8/C9/C10/C11/O1. The torsion angle values for selected atoms as observed for the molecule is shown below which proves the existence of flavanone ring in quasi chair conformation with phenyl ring at equatorial position and H-7 hydrogen at axial position. The values of final R indices R_1= 0.0691 and WR_2= 0.1634 indicates the crystal structure is well resolved.

Selected Atoms	**Torsion Angle**
H7-C7-C8-$H8_A$	-54.31
H7-C7-C8-$H8_B$	-171.97
C6-C7-C8-$H8_A$	66.51
C6-C7-C8-$H8_B$	-51.16
H7-C7-C6-C5	-81.77
H7-C7-C6-C1	95.76

Crystal structure data & structure refinement for the molecule is shown below:

Empirical formula	$C_{19}H_{15}ClO_3$
Formula weight	326.76
Temperature	273(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 14.401(3) Å $\alpha = 90°$ b = 5.4980(11) Å $\beta = 109.841(3)°$ c = 21.006(4)Å $\gamma = 90°$

Volume	1564.4(6) $Å^3$
Z	4
Density (calculated)	1.387 mg/m^3
Absorption coefficient ($\mu M_o K_\alpha$)	0.257 mm^{-1}
F(000)	680
Crystal size	0.24 x 0.15 x 0.10 mm
Theta range for data collection	1.50° to 28.26°
Index ranges	-18<=h<=19, -5<=k<=7, -26<=l<=26
Reflections collected	8544
Independent reflections	3574 [R(int) = 0.0311]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3574 / 0 / 210
Goodness-of-fit on F^2	1.085
Final R indices [$I>2\sigma(I)$]	R1 = 0.0691, wR2 = 0.1634
R indices (all data)	R1 = 0.0935, wR2 = 0.1765
Largest diff. peak and hole	0.421 and -0.234 $e.A^{-3}$

Crystallographic data (excluding structure factors) for the structure in this thesis have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number: **CCDC 621173**.

Table 1: Crystal data and structure refinement.

Identification code	7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one
Empirical formula	C19 H15 Cl O3
Formula weight	326.76
Temperature	273(2) K
Wavelength	0.71073 A
Crystal system	Monoclinic
Space group	P21/c
Unit cell dimensions	a = 14.401(3) A alpha = 90 deg. b = 5.4980(11) A beta = 109.841(3) deg. c = 21.005(4) A gamma = 90 deg.
Volume	1564.4(6) A^3
Z	4
Density (calculated)	1.387 Mg/m^3
Absorption coefficient	0.257 mm^-1
F(000)	680
Crystal size	0.24 x 0.15 x 0.10 mm
Theta range for data collection	1.50 to 28.26 deg.
Index ranges	-18<=h<=19, -5<=k<=7, -26<=l<=26
Reflections collected	8544
Independent reflections	3574 [R(int) = 0.0311]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3574 / 0 / 210
Goodness-of-fit on F^2	1.085
Final R indices [I>2sigma(I)]	R1 = 0.0691, wR2 = 0.1634
R indices (all data)	R1 = 0.0935, wR2 = 0.1765

Largest diff. peak and hole 0.421 and -0.234 e.A^-3

Table 2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Cl(1)	4082(1)	-7613(2)	3328(1)	66(1)
O(1)	2754(1)	-715(3)	622(1)	49(1)
O(3)	3329(1)	5931(3)	-645(1)	53(1)
C(9)	821(2)	-1282(5)	-335(1)	40(1)
C(10)	1488(2)	653(4)	-402(1)	38(1)
O(2)	16(1)	-1640(4)	-762(1)	55(1)
C(14)	1858(2)	3966(5)	-1014(1)	42(1)
C(11)	2444(2)	828(4)	80(1)	39(1)
C(6)	2506(2)	-3236(5)	1454(1)	41(1)
C(13)	2796(2)	4052(5)	-520(1)	43(1)
C(3)	3476(2)	-5957(5)	2603(1)	46(1)
C(8)	1196(2)	-2884(5)	281(1)	44(1)
C(15)	1198(2)	2228(4)	-952(1)	41(1)
C(12)	3131(2)	2539(5)	35(1)	45(1)
C(7)	1989(2)	-1673(5)	848(1)	44(1)
C(1)	2068(2)	-5262(5)	1622(1)	53(1)
C(2)	2542(2)	-6620(5)	2194(2)	57(1)
C(4)	3929(2)	-3944(6)	2449(1)	56(1)
C(5)	3444(2)	-2601(5)	1883(1)	56(1)
C(16)	1829(2)	5950(5)	-1475(1)	49(1)
C(17)	2709(2)	7024(5)	-1228(2)	56(1)
C(18)	4150(2)	2760(7)	556(2)	73(1)
C(19)	985(3)	6683(6)	-2084(2)	70(1)

Table 3: Bond lengths [A] and angles [deg].

Symmetry transformations used to generate equivalent atoms

Cl(1)-C(3)	1.734(3)
O(1)-C(11)	1.366(3)
O(1)-C(7)	1.439(3)
O(3)-C(13)	1.365(3)
O(3)-C(17)	1.384(3)
C(9)-O(2)	1.217(3)
C(9)-C(10)	1.472(3)
C(9)-C(8)	1.505(3)
C(10)-C(15)	1.390(3)

C(10)-C(11)	1.408(3)
C(14)-C(15)	1.384(3)
C(14)-C(13)	1.396(3)
C(14)-C(16)	1.450(4)
C(11)-C(12)	1.392(3)
C(6)-C(1)	1.383(4)
C(6)-C(5)	1.390(4)
C(6)-C(7)	1.507(4)
C(13)-C(12)	1.379(3)
C(3)-C(2)	1.376(4)
C(3)-C(4)	1.378(4)
C(8)-C(7)	1.498(3)
C(8)-H(8A)	0.9700
C(8)-H(8B)	0.9700
C(15)-H(15)	0.9300
C(12)-C(18)	1.508(4)
C(7)-H(7)	0.9800
C(1)-C(2)	1.383(4)
C(1)-H(1)	0.9300
C(2)-H(2)	0.9300
C(4)-C(5)	1.374(4)
C(4)-H(4)	0.9300
C(5)-H(5)	0.9300
C(16)-C(17)	1.333(4)
C(16)-C(19)	1.490(4)
C(17)-H(17)	0.9300
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-H(19A)	0.9600
C(19)-H(19B)	0.9600
C(19)-H(19C)	0.9600

C(11)-O(1)-C(7)	115.55(17)
C(13)-O(3)-C(17)	105.2(2)
O(2)-C(9)-C(10)	122.4(2)
O(2)-C(9)-C(8)	120.8(2)
C(10)-C(9)-C(8)	116.73(19)
C(15)-C(10)-C(11)	119.9(2)
C(15)-C(10)-C(9)	120.6(2)
C(11)-C(10)-C(9)	119.4(2)
C(15)-C(14)-C(13)	118.3(2)
C(15)-C(14)-C(16)	135.8(2)
C(13)-C(14)-C(16)	105.8(2)
O(1)-C(11)-C(12)	115.9(2)
O(1)-C(11)-C(10)	121.3(2)
C(12)-C(11)-C(10)	122.8(2)
C(1)-C(6)-C(5)	117.7(2)
C(1)-C(6)-C(7)	122.5(2)
C(5)-C(6)-C(7)	119.8(2)
O(3)-C(13)-C(12)	124.1(2)
O(3)-C(13)-C(14)	110.3(2)
C(12)-C(13)-C(14)	125.5(2)
C(2)-C(3)-C(4)	120.4(2)
C(2)-C(3)-Cl(1)	120.2(2)
C(4)-C(3)-Cl(1)	119.4(2)
C(7)-C(8)-C(9)	112.1(2)

C(7)-C(8)-H(8A)	109.2
C(9)-C(8)-H(8A)	109.2
C(7)-C(8)-H(8B)	109.2
C(9)-C(8)-H(8B)	109.2
H(8A)-C(8)-H(8B)	107.9
C(14)-C(15)-C(10)	119.1(2)
C(14)-C(15)-H(15)	120.4
C(10)-C(15)-H(15)	120.4
C(13)-C(12)-C(11)	114.3(2)
C(13)-C(12)-C(18)	122.7(2)
C(11)-C(12)-C(18)	123.0(2)
O(1)-C(7)-C(8)	111.3(2)
O(1)-C(7)-C(6)	105.92(18)
C(8)-C(7)-C(6)	116.3(2)
O(1)-C(7)-H(7)	107.7
C(8)-C(7)-H(7)	107.7
C(6)-C(7)-H(7)	107.7
C(2)-C(1)-C(6)	121.6(2)
C(2)-C(1)-H(1)	119.2
C(6)-C(1)-H(1)	119.2
C(3)-C(2)-C(1)	119.3(3)
C(3)-C(2)-H(2)	120.4
C(1)-C(2)-H(2)	120.4
C(5)-C(4)-C(3)	119.6(2)
C(5)-C(4)-H(4)	120.2
C(3)-C(4)-H(4)	120.2
C(4)-C(5)-C(6)	121.5(3)
C(4)-C(5)-H(5)	119.2
C(6)-C(5)-H(5)	119.2
C(17)-C(16)-C(14)	105.4(2)
C(17)-C(16)-C(19)	127.2(3)
C(14)-C(16)-C(19)	127.4(3)
C(16)-C(17)-O(3)	113.3(2)
C(16)-C(17)-H(17)	123.4
O(3)-C(17)-H(17)	123.4
C(12)-C(18)-H(18A)	109.5
C(12)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(12)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(16)-C(19)-H(19A)	109.5
C(16)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(16)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

Table 4: Anisotropic displacement parameters (A^2 x 10^3).

The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Cl(1)	66(1)	68(1)	59(1)	19(1)	17(1)	5(1)
O(1)	29(1)	61(1)	53(1)	15(1)	8(1)	-6(1)
O(3)	51(1)	56(1)	55(1)	1(1)	23(1)	-11(1)
C(9)	28(1)	44(1)	46(1)	-7(1)	11(1)	0(1)
C(10)	31(1)	41(1)	44(1)	-3(1)	13(1)	0(1)
O(2)	33(1)	64(1)	58(1)	-1(1)	2(1)	-9(1)
C(14)	43(1)	44(1)	41(1)	-2(1)	17(1)	4(1)
C(11)	32(1)	45(1)	41(1)	1(1)	12(1)	-1(1)
C(6)	41(1)	41(1)	42(1)	-5(1)	14(1)	-4(1)
C(13)	41(1)	47(1)	46(1)	-3(1)	21(1)	-6(1)
C(3)	50(1)	48(2)	42(1)	2(1)	19(1)	5(1)
C(8)	36(1)	44(1)	52(2)	-2(1)	14(1)	-6(1)
C(15)	31(1)	46(1)	41(1)	-6(1)	8(1)	2(1)
C(12)	31(1)	57(2)	46(1)	2(1)	11(1)	-5(1)
C(7)	33(1)	48(1)	49(1)	-4(1)	12(1)	-4(1)
C(1)	46(1)	51(2)	54(2)	0(1)	8(1)	-13(1)
C(2)	56(2)	52(2)	59(2)	6(1)	15(1)	-14(1)
C(4)	39(1)	71(2)	53(2)	8(1)	7(1)	-9(1)
C(5)	48(2)	60(2)	55(2)	9(1)	9(1)	-16(1)
C(16)	55(2)	48(2)	48(1)	2(1)	21(1)	6(1)
C(17)	65(2)	52(2)	59(2)	8(1)	34(2)	1(1)
C(18)	40(2)	96(3)	69(2)	16(2)	1(1)	-24(2)
C(19)	74(2)	70(2)	62(2)	16(2)	18(2)	6(2)

Table 5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3).

	x	y	z	U(eq)
H(8A)	651	-3304	434	53
H(8B)	1452	-4379	161	53
H(15)	570	2117	-1274	49
H(7)	1689	-301	1004	53
H(1)	1441	-5723	1342	63
H(2)	2233	-7967	2301	68
H(4)	4559	-3498	2728	68
H(5)	3751	-1235	1783	68
H(17)	2888	8373	-1427	67
H(18A)	4509	1278	568	109
H(18B)	4097	3053	993	109
H(18C)	4493	4088	438	109
H(19A)	1146	8163	-2265	105
H(19B)	409	6933	-1960	105
H(19C)	856	5423	-2419	105

3.B.3 Experimental

X-ray diffraction data were collected using Mo Kα (λ=0.71073A°) radiation on a SMART APEX diffractometer equipped with a CCD area detector. Data collection, data reduction, structure solution/refinement were carried out using the software package of SMART APEX. Graphics were generated using MERCURY 1.4.1.[2]

Single crystal X-ray diffraction

X-ray quality single crystals of **7-(4-chloro-phenyl)-3,9-dimethyl-6,7-dihydro-furo[3,2-*g*]chromen-5-one 7a** were grown in a slow evaporation condition at room temperature. Crystals were obtained from a mixture of ethanol and toluene. The structure was solved by direct methods and refined in a routine manner. All hydrogen atoms were geometrically fixed and refined.

3.B.4 Conclusions

- The flavanone ring in furoflavanones exists in quasi chair conformation.
- The phenyl ring is placed equatorial and parallel to the plane of the molecule.
- The R values are in acceptable range and indicate the crystal structure is well resolved.

3.B.5 References

1. Philbin, E. M. and Wheeler, T. S. *Proc. Chem. Soc.* London, **1958**, 167.
2. Mercury 1.4.1, supplied with Cambridge Structural Database, Cambridge Crystallographic Data Centre, Cambridge, UK, 2001.