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Synthesis, structural revision, and biological activities of 4′-chloroaurone, a metabolite of marine brown alga *Spatoglossum variabile*☆

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Abstract—4′-Chloroaurone (**1a**), the only aurone reported from a marine source, *Spatoglossum variabile* was synthesized from 2-hydroxyacetophenone along with six structural analogs. The products obtained were *Z*-isomers and these were converted into *E*-isomers by photoisomerization. The *E* and *Z* isomers of aurones showed distinct proton and carbon chemical shifts. However, the spectroscopic data of either *Z*-4′-chloroaurone (**1a**) or its *E*-isomer (**2a**) did not match with those reported for the natural product and thus requires revision of the structure assigned. The proton NMR spectroscopic data reported for the natural product matches with those reported for a known isocoumarin (**5**). The synthesized *E* and *Z* aurones were evaluated for their antioxidant and antibacterial activities. The aurone, *Z*-2-[(3,4-dihydroxyphenyl)methylene]benzo[*b*]furan-3-one exhibited significant antioxidant activity. Interestingly, *Z*-aurones are active against Gram-positive and Gram-negative bacteria, whereas the corresponding *E*-aurones were inactive.

1. Introduction

Aurones, [2-benzylidenebenzofuran-3(2*H*)-ones], are naturally occurring yellow pigments of plants and are structurally related to flavonoids.[1] In addition to this pigmentation role, aurones have been described as phytoalexins, used by the plant as defense agents against various infections. They found to exhibit antiviral, antiparasitic, antifungal, and antidiabetic activities.[2] Aurones are generally prepared by two main methods: (i) condensation between benzofuranones and benzaldehydes in the presence of acidic or basic reagents or neutral alumina[3,4] (ii) by oxidative cyclization of 2′-hydroxychalcones.[5–7] The only aurone isolated from the marine source, *Spatoglossum variabile* (brown alga),[8] was assigned the structure of 4′-chloroaurone (**1a**, Fig. 1), based on the interpretation of ^{1}H and ^{13}C NMR spectral data. The stereochemistry was assigned as *Z*, based on the calculation of heat of formations of both *Z* and *E* isomers by AM1 (the Austin model 1) method.[9,10]

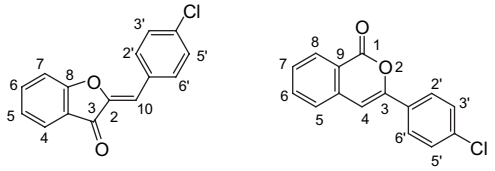

Figure 1. Structures of 4′-chloroaurone (**1a**) and 3-(4′-chloroisocoumarin) (**5**).

Marine natural products are emerging as potential candidates for the treatment of cancer and other ailments.[11] The presence of halogen substituents is unique for marine metabolites while it is rare for compounds obtained from terrestrial sources. Although stereochemistry plays a major role in the drug discovery and development, the biological activities of aurones were not studied in detail with respect to their double bond geometry (*E*/*Z*). In view of the above and due to our interest in aurones and isoaurones,[12,13] we have synthesized **1a** along with six new structural analogs. The *E*-aurones were obtained from *Z*-aurones by photoisomerization and studied their antioxidant and antibacterial activities. In this paper, we report the details of their synthesis, stereochemical assignments, structure revision, and antioxidant and antibacterial acitivities of aurones.

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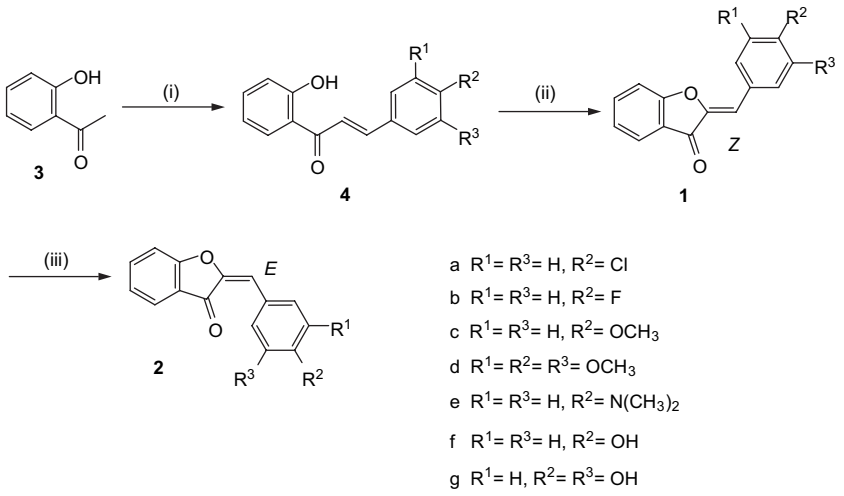

Scheme 1. Reagents and conditions: (i) substituted benzaldehydes, KOH, EtOH, rt, 18 h, 60–70% yield; (ii) $Hg(OAc)_2$, pyridine, reflux, 1 h, 40–79% yield; and (iii) UV, methanol, 12 h, 26–60% yield.

2. Results and discussion

2.1. Synthesis

The classical Claisen–Schmidt reaction was utilized effectively for the synthesis of chalcones in good yield.[14,15] 2-Hydroxyacetophenone (**3**) was treated with 4-chlorobenzaldehyde in the presence of ethanolic potassium hydroxide at 25 °C for 14 h gave 2-hydroxy-4′-chlorochalcone (**4a**) in 70% yield (Scheme 1). The other chalcones (**4b–g**) were prepared in the same manner. Sekizaki[16] has reported the oxidative cyclization of chalcones to aurones accompanied by flavanones using mercury(II) acetate in acetic acid. We modified the procedure and the chalcones (**4a–g**) were cyclized using mercury(II) acetate in pyridine to give only aurones (**1a–g**) in good yields. In all cases, a single geometric isomer (*Z*) was obtained and confirmed by analysis of their proton and carbon NMR spectra. It is known that the *Z*-isomer is thermodynamically more stable than *E*-isomer.[17] The *Z*-aurones (**1a–d**) were photoisomerized to *E*-isomers with a Rayonet photoreactor.

2.2. Stereochemical assignments

The selected proton NMR spectroscopic data of *Z* and *E* aurones are presented in Table 1. It is known from the literature that the assignment of configuration in aurones is possible on the basis of the chemical shifts of the vinylic proton.[17] The present study also reveals that the vinylic proton (H-10) in the *E*-isomers gives a singlet as expected at a lower field than the corresponding proton in *Z*-isomers due to the anisotropy of carbonyl group, but the difference is small (0.04–0.10 ppm). However, we have found that in all *E*-isomers, the protons (H-2′ and H-6′) of the pendant aryl unit appeared as a doublet at lower field than the corresponding protons in *Z*-isomers and this chemical shift difference is large enough (0.27–0.49 ppm) to assign the stereochemistry at the double bond, reliably.

The ^{13}C NMR data of *Z* and *E* aurones (Table 2) revealed that the chemical shift differences of olefinic carbon (C-10) is negligible, but in all *E*-isomers the C-2 resonances (δ 147.1–148.3) are at a lower field than the corresponding *Z*-isomers (δ 145.9–146.5) and this difference (>1.2 ppm) could be used to differentiate the isomers.[18,19] Further, in the case of *Z*-isomers, the carbonyl absorption (δ 184.1–184.5) is at a lower field than the corresponding carbonyl resonances of *E*-isomers (δ 182.5–182.8) and this difference (>1.3 ppm) could also be used to assign the configuration at the double bond in aurones.

2.3. Structural revision

The *Z* and *E* isomers of synthetic 4′-chloroaurone were obtained as light yellow colored compounds with mp 156–158 °C (*Z*-isomer) and 148–150 °C (*E*-isomer), but the natural 4′-chloroaurone was reported as a colorless compound with mp 205 °C.[8]

The IR spectrum of synthetic *Z*-4′-chloroaurone (**1a**) showed two absorptions at 1708 and 1652 cm^{-1} due to the presence of α,β-unsaturated system. While its *E*-isomer (**2a**) showed absorptions at 1686 and 1630 cm^{-1}. But the IR absorption of natural 4′-chloroaurone was reported at 1721 cm^{-1}.

Table 1. Selected ^1H NMR spectroscopic data of *Z* and *E* aurones (δ ppm)

Compd	*Z*-Aurones (**1**)		*E*-Aurones (**2**)	
	H-10	H-2′,6′	H-10	H-2′,6′
a	6.82	7.84	6.88	8.11
b	6.86	7.92	6.90	8.20
c	6.89	7.90	6.93	8.23
d	6.82	7.19	6.92	7.68

Table 2. Selected ^{13}C NMR data of *Z* and *E* aurones (δ ppm)

Compd	*Z*-Aurones (**1**)			*E*-Aurones (**2**)		
	C-2	C-10	C=O	C-2	C-10	C=O
a	146.5	111.1	184.1	148.3	112.6	182.8
b	146.5	111.7	184.5	147.8	112.6	182.7
c	145.9	112.8	184.5	147.1	112.5	182.5
d	146.5	112.9	184.5	147.8	112.5	182.7

Table 3. ^{1}H and ^{13}C NMR data of synthetic **1a**, **2a**, and natural 4′-chloroaurone

Position	**1a**[a]		**2a**[a]		Natural 4′-chloroaurone[b]	
	δ_H (ppm)	δ_C (ppm)	δ_H (ppm)	δ_C (ppm)	δ_H (ppm)	δ_C (ppm)
2		146.5		148.3		152.7
3		184.1		182.8		182.0
4	7.80 (d, 7.7)	123.2	7.70 (d, 7.9)	122.9	8.28 (dd, 7.0, 1.0)	129.6
5	7.23 (t, 7.7)	124.3	7.17 (t, 7.9)	124.7	7.69 (dt, 7.0, 1.1)	135.0
6	7.67 (t, 7.7)	136.6	7.62 (t, 7.9)	136.9	7.47 (dt, 7.0, 1.1)	126.0
7	7.33 (d, 7.7)	112.5	7.19 (d, 7.9)	121.1	7.49 (dd, 7.0, 1.1)	128.4
8		165.6		165.3		162.0
9		121.0		123.2		120.7
10	6.82 (s)	111.1	6.88 (s)	112.6	6.91 (s)	102.0
1′		130.3		130.4		130.5
2′,6′	7.84 (d, 8.4)	132.1	8.11 (d, 8.4)	132.1	7.79 (d, 8.5)	126.5
3′,5′	7.42 (d, 8.4)	128.7	7.39 (d, 8.4)	128.7	7.42 (d, 8.5)	129.1
4′		135.4		136.2		137.3

Coupling constants (J in Hz) are in parentheses.
[a] ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) in $CDCl_3$.
[b] ^{1}H (500 MHz) and ^{13}C NMR data (75 MHz) in $CDCl_3$ are taken from Ref. 8.

The ^{1}H and ^{13}C NMR spectral data of synthetic *Z*-4′-chloroaurone, *E*-4′-chloroaurone, and the natural 4′-chloroaurone are given in Table 3. The ^{1}H NMR data of the natural compound did not match with either *Z* or *E*-isomer (Table 3). The chemical shifts of H-4 (δ 8.28) and H-10 (δ 6.91) of natural compound are not consistent with either *Z*-isomer (**1a**) or *E*-isomer (**2a**). Although the chemical shift of the carbonyl carbon of natural product (δ 182.0) is close to the carbonyl carbon of synthetic *E*-isomer (**2a**, δ 182.8), but the vinylic carbon of natural product (δ 102.2) is not corroborative with *E*-isomer (**2a**, δ 112.6) or *Z*-isomer (**1a**, δ 111.1). The other proton and carbon NMR data of the natural compound are inconsistent with either *E*-isomer (**2a**) or *Z*-isomer (**1a**). Based on the differences in physical and spectroscopic (IR, ^{1}H NMR, and ^{13}C NMR) data of natural **1a** with those of either synthetic **1a** or **2a**, it is concluded that the structure proposed for marine natural metabolite requires revision.

After careful analysis of the spectroscopic data reported for 4′-chloroaurone, we have found that the reported proton NMR data agrees well with those of an isocoumarin **5**[20] (Fig. 1). The proton NMR data reported for 4′-chloroaurone have been reassigned and the data are found to be in good agreement with the reported data[20] of 3-(4′-chlorophenyl)-isocoumarin (Table 4). Unfortunately, carbon NMR data for this compound are not available to compare with the carbon chemical shifts reported for natural aurone. As such further study is required to confirm the revised structure.

Table 4. ^{1}H NMR data of 4′-chloroaurone (reassigned) and isocoumarin **5**

Position	4′-Chloroaurone[a]	Isocoumarin **5**[b]
	δ (ppm)	δ (ppm)
4	6.91 (s)	6.91 (s)
5	7.49 (dd, 7.0, 1.1)	7.49 (m)
6	7.69 (dt, 7.0, 1.1)	7.71 (dt, 7.6, 1.3)
7	7.47 (dt, 7.0, 1.1)	7.49 (m)
8	8.28 (dd, 7.0, 1.0)	8.29 (d, 6.9)
2′,6′	7.79 (d, 8.5)	7.80 (d, 8.7)
3′,5′	7.42 (d, 8.5)	7.42 (d, 8.7)

Coupling constants (J in Hz) are in parentheses.
[a] ^{1}H NMR data (500 MHz) in $CDCl_3$ are taken from Ref. 8 and reassigned.
[b] ^{1}H NMR data (500 MHz) in $CDCl_3$ are taken from Ref. 20.

2.4. Antioxidant activity

Superoxide radical scavenging activity. Superoxide radicals were generated in vitro by non-enzymatic system and determined spectrophotometrically (560 nm) by nitro blue tetrazolium (NBT) photoreduction method.[21,22] The antioxidant activity of *Z* and *E* aurones was expressed as 50% inhibitory concentration (IC_{50} in μM). The aurone, *Z*-2-[(3,4-dihydroxyphenyl)methylene]benzo[*b*]furan-3-one having catechol moiety exhibited good activity (IC_{50}: 22.2 μM) and was several times potent than the commercial antioxidants like Vitamin C (IC_{50}: 852 μM) and BHA (IC_{50}: 966 μM). The superior scavenging ability of this aurone lends further support to the fact that the catechol system enhances the antioxidant activity.[23] The other aurones did not show any appreciable activity.

2.5. Antibacterial activity

To check the importance of stereochemistry of aurones to their activity, we have screened the antibacterial activity of *Z* and *E* aurones. The activity was determined using agar-cup plate diffusion method[24] against the Gram-positive organisms (*Bacillus subtilis*, *Staphylococcus epidermidis*, *Staphylococcus aureus*) and Gram-negative organisms (*Escherichia coli*, *Salmonella aboni*). The results are summarized in Table 5. The data revealed that the

Table 5. Antibacterial activity of *Z* and *E* aurones at a concentration of 200 μg/0.05 mL, zone of inhibition (mm)

Compd	*B. subtilis*	*S. epidermidis*	*S. aureus*	*E. coli*	*S. aboni*
1a	—	—	—	—	—
2a	—	—	—	—	—
1b	12.0	8.0	9.0	—	—
2b	—	—	—	—	—
1c	11.0	9.0	10.0	—	—
2c	—	—	—	—	—
1d	14.0	9.0	12.0	—	—
2d	—	—	—	—	—
1e	9.0	8.0	10.0	—	—
1f	18.0	11.0	9.0	10.0	9.0
1g	16.0	12.0	8.5	—	—
Cipr	19.0	17.0	14.0	14.0	19.0

Cipr: Ciprofloxacin (0.5 μg/0.05 mL).
—: No significant antibacterial activity.

Z-hydroxyaurones (**1f** and **1g**) and trimethoxyderivative (**1d**) exhibited potent antibacterial activity. It is interesting to note that the *Z*-aurones (**1b**, **1c**, and **1d**) exhibited good activity, whereas the corresponding *E*-isomers (**2b**, **2c**, and **2d**) did not exhibit any appreciable activity, even at a concentration of 500 μg/0.05 mL. Therefore, *Z*-stereochemistry is important for the antibacterial activity shown by the aurones.

3. Conclusions

In summary, we have accomplished the synthesis of the proposed structure for 4′-chloroaurone (**1a**), the only aurone isolated from a marine source *S. variabile* in addition to six structural analogs. The *Z*-isomers were converted into *E*-isomers and assigned the stereochemistry at the double bond based on proton and carbon NMR data. The spectral data of synthetic **1a** or **2a** did not match with those reported for 4′-chloroaurone. The reported proton NMR data of natural product have been reassigned and found to match well with those reported for an isocoumarin **5**. The aurone, *Z*-2-[(3,4-dihydroxyphenyl)methylene]benzo[*b*]furan-3-one exhibits potent antioxidant activity. The *Z*-stereochemistry is important for the antibacterial activity.

4. Experimental

4.1. General

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. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) spectra were recorded on a Bruker spectrometer using TMS as an internal reference and the values for chemical shifts (δ) being given in parts per million and coupling constants (J) in hertz (Hz). In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined using DEPT-135, and are given in parentheses. Mass spectra were recorded on Agilent 1100 LC/MSD and elemental analysis on a Vario El Elementar instrument. The test organisms for antibacterial activity studies, *B. subtilis*, *S. aureus*, *S. epidermidis*, *E. coli*, *S. aboni* were obtained from National Collection of Industrial Microorganism, India. The chalcones (**4a**–**g**) were prepared by the standard procedure and their spectroscopic data are consistent with the literature values.[25–28] For antioxidant activity procedure see Ref. 29 and antibacterial activity procedure see Ref. 24.

4.1.1. General procedure for the preparation of *Z*-aurones (1). To a solution of mercuric acetate (319 mg, 1 mmol) in pyridine (10 mL) was added chalcone (1 mmol) at rt and the mixture was refluxed for 1 h. The cooled reaction mixture was poured into ice cold water (50 mL) and acidified with dil HCl. The precipitated solid was filtered, washed with cold water, and dried to give the products, which were recrystallized from chloroform–methanol.

4.1.1.1. *Z*-2-[(4-Chlorophenyl)methylene]benzo[*b*]furan-3-one (1a). Light yellow powder, 202 mg (79%), mp 156–158 °C; IR (Neat): 2923, 1708, 1652, 1299, 1188, 1091, 884 cm^{-1}; ^{1}H and ^{13}C NMR ($CDCl_3$): see Table 3; LCMS (ESI, positive scan): *m*/*z* 257, 259 $(M+H)^+$. Analysis found: C, 70.15; H, 3.55%. Calcd for $C_{15}H_9ClO_2$: C, 70.19; H, 3.53%.

4.1.1.2. *Z*-2-[(4-Fluorophenyl)methylene]benzo[*b*]furan-3-one (1b). Light yellow powder, 168 mg (70%), mp 162–164 °C; IR (Neat): 1703, 1656, 1598, 1299, 1236, 1187, 1125, 1096, 1015, 952 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.92 (2H, dd, J=8.6, 5.7 Hz, H-2′,6′), 7.81 (1H, d, J=7.6 Hz, H-4), 7.66 (1H, t, J=7.6 Hz, H-6), 7.33 (1H, d, J=7.6 Hz, H-7), 7.23 (1H, t, J=7.6 Hz, H-5), 7.15 (2H, dd, J=8.6 Hz, H-3′,5′), 6.86 (1H, s, H-10); ^{13}C NMR ($CDCl_3$): δ 184.5 (C-3), 166.1 (C-8), 163.4 (d, $^1J_{CF}$=252 Hz, C-4′), 146.5 (C-2), 136.9 (C-6), 133.5 (d, $^3J_{CF}$=8 Hz, C-2′,6′), 128.6 (d, $^4J_{CF}$=3 Hz, C-1′), 124.7 (C-5), 123.5 (C-4), 121.6 (C-9), 116.1 (d, $^2J_{CF}$=22 Hz, C-3′,5′), 112.9 (C-7), 111.7 (C-10); LCMS (ESI, positive scan): *m*/*z* 241 $(M+H)^+$. Analysis found: C, 74.75; H, 4.04%. Calcd for $C_{15}H_9FO_2$: C, 75.00; H, 3.78%.

4.1.1.3. *Z*-2-[(4-Methoxyphenyl)methylene]benzo[*b*]furan-3-one (1c). Light yellow powder, 164 mg (69%), mp 140–141 °C; IR (Neat): 2921, 1698, 1644, 1588, 1298, 1265, 1182, 1130, 1110, 1097, 1018, 884 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.90 (2H, d, J=8.8 Hz, H-2′,6′), 7.81 (1H, d, J=7.8 Hz, H-4), 7.64 (1H, t, J=7.8 Hz, H-6), 7.32 (1H, d, J=7.8 Hz, H-7), 7.21 (1H, t, J=7.8 Hz, H-5), 6.98 (2H, d, J=8.8 Hz, H-3′,5′), 6.89 (1H, s, H-10), 3.87 (3H, s, Ar–OCH_3); ^{13}C NMR ($CDCl_3$): δ 184.5 (C-3), 165.9 (C-8), 161.1 (C-4′), 145.9 (C-2), 136.5 (C-6), 133.4 (C-2′,6′), 125.1 (C-1′), 124.5 (C-5), 123.2 (C-4), 122.0 (C-9), 114.5 (C-3′,5′), 113.3 (C-7), 112.8 (C-10), 55.4 (Ar–OCH_3); LCMS (ESI, positive scan): *m*/*z* 253 $(M+H)^+$. Analysis found: C, 76.15; H, 4.82%. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79%.

4.1.1.4. *Z*-2-[(3,4,5-Trimethoxyphenyl)methylene]benzo[*b*]furan-3-one (1d). Light yellow powder, 225 mg (72%), mp 174–176 °C; IR (Neat): 2924, 1703, 1646, 1600, 1296, 1245, 1189, 1127, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.81 (1H, dd, J=7.7, 1.1 Hz, H-4), 7.66 (1H, td, J=7.7, 1.1 Hz, H-6), 7.31 (1H, d, J=7.7 Hz, H-7), 7.23 (1H, t, J=7.7 Hz, H-5), 7.19 (2H, s, H-2′,6′), 6.82 (1H, s, H-10), 3.95 (6H, s, 2×Ar–OCH_3), 3.92 (3H, s, Ar–OCH_3); ^{13}C NMR ($CDCl_3$): δ 184.5, 165.9, 153.4, 146.5, 140.3, 136.7, 127.7, 124.7, 123.6, 121.8, 113.3, 112.9, 109.2; LCMS (ESI, positive scan): *m*/*z* 313 $(M+H)^+$. Analysis found: C, 69.18; H, 5.19%. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16%.

4.1.1.5. *Z*-2-[(4-*N*,*N*-Dimethylaminophenyl)methylene]benzo[*b*]furan-3-one (1e). Light yellow powder, 160 mg (60%), mp 174–176 °C; IR (Neat): 2913, 1691, 1639, 1607, 1298, 1184, 1150, 1135, 1111, 1096, 952 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.85 (2H, d, J=8.8 Hz, H-2′,6′), 7.80 (1H, d, J=8.2 Hz, H-4), 7.60 (1H, td, J=8.2, 1.1 Hz, H-6), 7.31 (1H, d, J=8.2 Hz, H-7), 7.18 (1H, td, J=8.2, 1.1 Hz, H-5), 6.92 (1H, s, H-10), 6.75 (2H, d, J=8.8 Hz, H-3′,5′), 3.08 (6H, s, Ar–$N(CH_3)_2$); ^{13}C NMR ($CDCl_3$): δ 183.8, 165.3, 151.4, 145.0, 135.7, 133.7, 124.2, 122.8, 122.5, 120.1, 115.2, 112.7, 112.1, 40.0; LCMS (ESI, positive scan): *m*/*z* 266 $(M+H)^+$. Analysis found: C, 76.74; H, 5.65%. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H,

5.70%. HRMS (*m*/*z*) Found: 266.1184, calcd for $C_{17}H_{15}NO_2$ (M+H): 266.1181.

4.1.1.6. *Z*-2-[(4-Hydroxyphenyl)methylene]benzo[*b*]-furan-3-one (1f). Light yellow powder, 167 mg (70%), mp 261–263 °C; IR (KBr): 3431, 1686, 1642, 1612, 1288, 1173, 1132, 884 cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 7.81 (2H, d, J=8.4 Hz, H-2′,6′), 7.75 (1H, d, J=7.6 Hz, H-4), 7.68 (1H, t, J=7.6 Hz, H-6), 7.37 (1H, d, J=7.6 Hz, H-7), 7.23 (1H, t, J=7.6 Hz, H-5), 6.93 (2H, d, J=8.4 Hz, H-3′,5′), 6.83 (1H, s, H-10); ^{13}C NMR ($CDCl_3$+DMSO-d_6): δ 182.9, 164.5, 158.8, 144.2, 135.5, 132.6, 123.1, 122.3, 120.8, 115.3, 115.1, 112.8, 111.9; LCMS (ESI, negative scan): *m*/*z* 237 $(M-H)^-$. Analysis found: C, 75.59; H, 4.25%. Calcd for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23%. HRMS (*m*/*z*) Found: 239.0704, calcd for $C_{15}H_{10}O_3$ (M+H): 239.0708.

4.1.1.7. *Z*-2-[(3,4-Dihydroxyphenyl)methylene]benzo-[*b*]furan-3-one (1g). Light yellow powder, 102 mg (40%), mp 218–220 °C; IR (KBr): 3441, 3278, 1697, 1649, 1585, 1295, 1189, 1132, 886 cm^{-1}; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 7.76 (d, J=7.4 Hz, H-4), 7.66 (1H, t, J=7.4 Hz, H-6), 7.57 (1H, dd, J=8.0, 1.2 Hz, H-6′), 7.30–7.35 (2H, m, H-7,2′), 7.22 (1H, t, J=7.4 Hz, H-5), 6.90–6.94 (1H, m, H-5′), 6.79 (1H, s, H-10); ^{13}C NMR ($CDCl_3$+DMSO-d_6): δ 183.4, 164.8, 147.4, 144.6, 135.8, 124.6, 123.5, 123.3, 122.5, 121.2, 117.8, 117.4, 115.4, 113.7, 112.1; LCMS (ESI, negative scan): *m*/*z* 253 $(M-H)^-$. Analysis found: C, 70.82; H, 3.99%. Calcd for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96%.

4.1.2. General procedure for the preparation of *E*-aurones (2). A solution of *Z*-aurones (**1**, 1.0 g) in methanol (500 mL) was irradiated using Rayonet reactor at 350 nm for 12 h. The solvent was evaporated under reduced pressure and the residue was chromatographed over silica gel column using hexane–ethyl acetate mixtures as eluents to give the *E*-aurones.

4.1.2.1. *E*-2-[(4-Chlorophenyl)methylene]benzo[*b*]-furan-3-one (2a). Light yellow powder, 550 mg (55%), mp 148–150 °C; IR (Neat): 1686, 1630, 1589, 1237, 1197, 1081, 1018, 963, 896 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$): see Table 3; LCMS (ESI, positive scan): *m*/*z* 257, 259 $(M+H)^+$. Analysis found: C, 70.41; H, 3.66%. Calcd for $C_{15}H_9ClO_2$: C, 70.19; H, 3.53%.

4.1.2.2. *E*-2-[(4-Fluorophenyl)methylene]benzo[*b*]-furan-3-one (2b). Light yellow powder, 510 mg (51%), mp 156–158 °C; IR (Neat): 1688, 1620, 1600, 1240, 1165, 1082, 960, 897 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.20 (2H, dd, J=8.6, 5.2 Hz, H-2′,6′), 7.77 (1H, d, J=7.9 Hz, H-4), 7.61 (1H, td, J=7.9, 1.1 Hz, H-6), 7.19 (1H, d, J=7.9 Hz, H-7), 7.17 (1H, t, J=7.9 Hz, H-5), 7.10 (2H, dd, J=8.6 Hz, H-3′,5′), 6.90 (1H, s, H-10); ^{13}C NMR ($CDCl_3$): δ 182.7 (C-3), 165.3 (C-8), 163.8 (d, $^1J_{CF}$=250 Hz, C-4′), 147.8 (C-2), 136.8 (C-6), 133.1 (d, $^3J_{CF}$=9 Hz, C-2′,6′), 128.2 (d, $^4J_{CF}$=4 Hz, C-1′), 124.6 (C-5), 123.3 (C-9), 122.8 (C-4), 121.4 (C-7), 115.5 (d, $^2J_{CF}$=22 Hz, C-3′,5′), 112.6 (C-10); LCMS (ESI, positive scan): *m*/*z* 241 $(M+H)^+$. Analysis found: C, 75.06; H, 3.90%. Calcd for $C_{15}H_9FO_2$: C, 75.00; H, 3.78%.

4.1.2.3. *E*-2-[(4-Methoxyphenyl)methylene]benzo[*b*]-furan-3-one (2c). Light yellow powder, 600 mg (60%), mp 98–100 °C; IR (Neat): 1681, 1629, 1605, 1262, 1181, 1080, 1027, 961, 895 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.23 (2H, d, J=8.8 Hz, H-2′,6′), 7.78 (1H, d, J=8.0 Hz, H-4), 7.60 (1H, t, J=8.0 Hz, H-6), 7.19 (1H, d, J=8.0 Hz, H-7), 7.16 (1H, t, J=8.0 Hz, H-5), 6.95 (2H, d, J=8.8 Hz, H-3′,5′), 6.93 (1H, s, H-10), 3.86 (3H, s, Ar–OCH_3); ^{13}C NMR ($CDCl_3$): δ 182.5 (C-3), 165.0 (C-8), 161.6 (C-4′), 147.1 (C-2), 136.3 (C-6), 133.1 (C-2′,6′), 124.9 (C-1′), 124.5 (C-5), 123.7 (C-9), 123.2 (C-4), 122.5 (C-7), 114.0 (C-3′,5′), 112.5 (C-10), 55.4 (Ar–OCH_3); LCMS (ESI, positive scan): *m*/*z* 253 $(M+H)^+$.

4.1.2.4. *E*-2-[(3,4,5-Trimethoxyphenyl)methylene]-benzo[*b*]furan-3-one (2d). Light yellow powder, 260 mg (26%), mp 105–106 °C; IR (Neat): 2940, 1688, 1630, 1601, 1299, 1244, 1190, 1127, 1085, 1005, 948, 867 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.80 (1H, d, J=7.9 Hz, H-4), 7.68 (2H, s, H-2′,6′), 7.63 (1H, td, J=7.9, 1.1 Hz, H-6), 7.21 (1H, d, J=7.9 Hz, H-7), 7.18 (1H, t, J=7.9 Hz, H-5), 6.92 (1H, s, H-10), 3.98 (6H, s, 2×Ar–OCH_3), 3.93 (3H, s, Ar–OCH_3); ^{13}C NMR ($CDCl_3$): δ 182.7 (C-3), 165.1 (C-8), 152.9 (C-3′,5′), 147.8 (C-2), 140.7 (C-4′), 136.6 (C-2′,6′), 127.5 (C-1′), 124.5 (C-6), 123.7 (C-5), 123.5 (C-9), 122.7 (C-4), 112.5 (C-10), 108.8 (C-7), 60.9 (Ar–OCH_3), 56.3 (2×Ar–OCH_3); LCMS (ESI, positive scan): *m*/*z* 313 $(M+H)^+$. Analysis found: C, 69.22; H, 5.95%. Calcd for $C_{18}H_{16}O_5$: C, 70.79; H, 5.95%.

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