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Synthesis and Antimicrobial Activity of (*Z*)-3-{[3-Oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one Derivatives[1]

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Abstract—A series of (*Z*)-3-{[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one derivatives have been synthesized from 2-hydroxyl acetophenones by the Vilesmeier–Haack reaction, Claisen–Schmidt reaction and mercury(II) acetate/cupric bromide. All the synthesized compounds were characterized by IR, ^{1}H and ^{13}C NMR, and mass spectral data and elemental analysis. The products were tested for their in vitro antimicrobial activity.

Keywords: aurones, chromanones, benzofurans, Vilesmeier–Haack reaction, Claisen–Schmidt reaction, mercury(II) acetate–cupric bromide, antimicrobial activity

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INTRODUCTION

Aurones [(*Z*)-2-benzylidenebenzofuran-3-(2*H*)-ones] constitute a less studied subclass of flavonoids, that rarely occur in nature. Aurones are responsible for pigmentation of flowers, especially bright yellow color, and fruits. Aurones and their synthetic analogues were determined to be promising bioactive compounds with anticancer [1, 2], antimicrobial [3], antioxidants [4, 5], enzyme inhibitory [6, 7], and enzyme-inducing activity [8].

Chromanones (4*H*-benzopyran-4-one) are widely spread in nature, compounds that demonstrate anti-cancer [9], antifungal [10, 11], antioxidant [12], and anti-HIV [13] activities. The compounds previously synthesized by direct coupling of benzofuranones with chromanones were associated with long reactions times, tedious work up procedures and low yields. Recently the microwave assisted organic synthesis became the promising alternative to conventional methods as effective, safe, economical, and eco-friendly [14]. In view of the potential bioactivity and improvement of synthetic methods for chromanone substituted aurones, in the current study (*Z*)-3-{[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one derivatives were synthesised from the respective chalcones (Scheme 1).

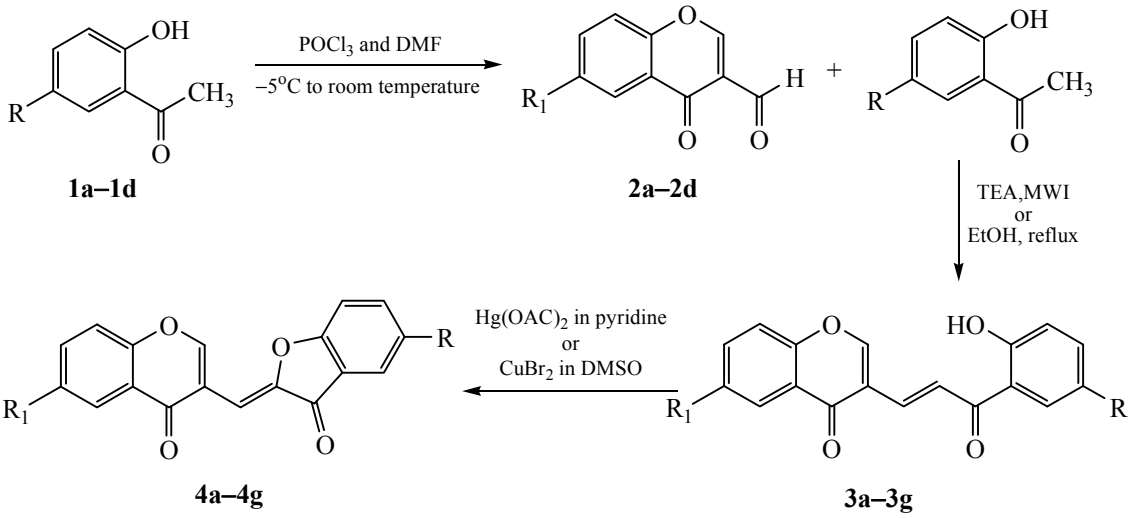
RESULTS AND DISCUSSION

Compounds **2a–2d** were synthesized from substituted-2-hydroxy acetophenones **1a–1d** by using the Vilsmeier Haack reagent ($POCl_3$ and DMF) at room temperature. Compounds **3a–3g** were synthesized by condensation of 4-oxo-4*H*-chromene-3-carbaldehydes **2a–2d** with substituted-2-hydroxy acetophenones in the presence of TEA and ethanol under microwave irradiation and conventional heating methods. In case of microwave irradiation, optimum results were achieved by irradiating at 160 Watts for 4–5 min with 30 s intervals (Table 1). Chalcones **3a–3g** reaction with Hg(II) acetate in pyridine or $CuBr_2$ in DMSO gave 3-[(*Z*)-[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-ones **4a–4g**. The processes that involved $CuBr_2$ in DMSO gave lower yields than Hg(II) acetate in pyridine (Table 2).

Biological activity. *Antimicrobial activity.* Antimicrobial activity of compounds **4a–4g** has been assayed within concentration range of 1 to 100 μg/mL against gram positive and gram negative clinically important

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

Scheme 1. Synthesis of 3-{(*Z*)-[3-oxobenzofuran-2(3*H*)ylidene]methyl}-4*H*-chromen-4-ones (**4a–4g**).



pathogens. Primarily, the Muller–Hinton agar method was used. The tests indicated antibacterial activity against all tested bacteria for compounds **4a**, **4c**, **4e,** and **4f**.

The minimum inhibitory concentration (MIC, μg/mL) of synthesized compounds **4a–4g** was determined to be much lower than that of Ciprofloxacin and Gentamicin (Table 3).

Table 1. Physical data for (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-one (**3a–3g**)

Compound no.	R	R^I	mp, °C	Conventional heating		Microwave irradiation	
				time, h	yield, %	time, min	yield, %
3a	H	H	179–181	3.0	68	4	80
3b	Me	H	182–184	3.0	70	4	83
3c	Me	Me	198–200	3.2	70	5	83
3d	Br	H	220–222	2.8	69	5	83
3e	Br	Br	233–235	3.0	65	5	80
3f	Cl	H	212–214	3.5	70	5	85
3g	Cl	Cl	229–231	3.0	70	5	84

Table 2. Physical data for 3-{(Z)-[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-ones (**4a–4g**)

Compound no.	R	R^I	mp, °C	Yield, %	
				$Hg(OAc)_2$ in pyridine	$CuBr_2$ in DMSO
4a	H	H	222	85	74
4b	Me	H	226	80	78
4c	Me	Me	227–229	78	70
4d	Br	H	274–276	82	72
4e	Br	Br	284–286	80	78
4f	Cl	H	264–268	79	77
4g	Cl	Cl	277–279	77	70

Table 3. Minimum inhibitory activity of the products

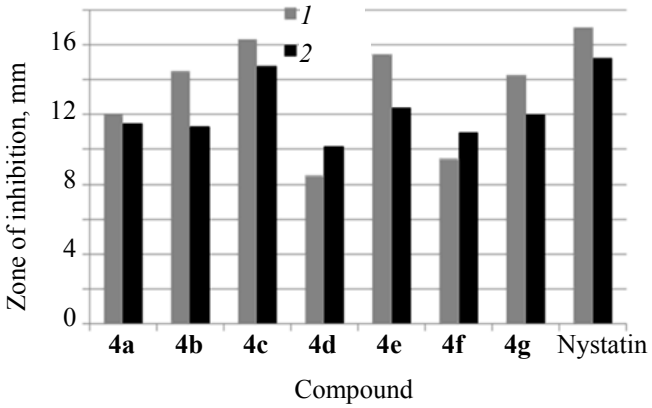
Compound	MIC value, μg/mL				
	Escherichia coli	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Streptococcus pyogenes*
4a	10.5±0.02	17.5±0.98	6.5±0.44	2.5±0.97	18.5±0.53
4b	19.5±0.13	11.5±0.66	13.5±0.28	12.5±0.66	1.5±0.65
4c	12.5±1.32[a]	7.5±0.32[a]	0.5±0.76[a]	0.5±0.62[a]	11.5±0.92
4d	7.5±1.08[a]	4.5±0.43[a]	4.0±0.78[a]	9.5±0.55[a]	10.5±0.53
4e	11.5±0.76	11.5±2.45	10.5±0.22	10.5±0.11[a]	10.5±0.41[a]
4f	12.5±0.65	10.5±1.65	12.5±0.86	11.5±0.2.43	16.5±0.83
4g	8.5±2.22[a]	10.0±2.45	7.5±0.54[a]	17.5±0.43	10.5±0.59[a]
Ciprofloxacin	8.2±4.08	4.5±1.34	8.08±0.79	8.12±0.75	9.5±0.11
Gentamicin	1.5±1.08	2.5±0.98	2.5±0.43	6.5±0.31	6.5±0.48

[a] Indicates statistically significant compared with Ciprofloxacin and Gentamicin ($p \leq 0.05$).

Table 4. Minimum inhibitory concentration of synthesized compounds

Compound	Concentration, μg/mL	Zone of inhibition, mm		MIC value, μg/mL	
		Aspergillus niger	*Aspergillus flavus*	*Aspergillus niger*	*Aspergillus flavus*
4a	10	12.22±1.23	1.45±0.53	8.50±0.26	10.0±0.67
4b	10	14.15±0.54	11.28±0.88	6.50±0.97[a]	10.50±0.88
4c	10	16.30±0.03	14.75±0.55	4.50±0.63[a]	5.50±0.44[a]
4d	10	8.50±0.42	10.15±0.73	9.50±0.43	9.59±0.35[a]
5e	10	15.45±0.05	12.40±0.52	5.0±0.83[a]	8.5.0±0.62[a]
4f	10	9.50±0.21	10.95±0.18	6.50±0.62[a]	8.50±0.72[a]
4g	10	14.25±0.42	11.98±0.89	5.5±0.78[a]	9.0±0.81[a]
Nystatin	50	17.0±0.48	15.20±0.28	5.50±0.18	7.80±0.67

[a] Indicates statistically significant compared with Nystatin ($p \leq 0.05$).



Zone of inhibition of antifungal activity: (1) *Aspergillus niger* and (*2*) *Aspergillus flavus.*

Antifungal activity. Zones of inhibition for compounds **4a–4g** were assayed *in vitro* at concentration of 10 μg/mL against *Aspergillus niger* and *Aspergillus flavus* (see figure). According to the accumulated data the compounds **4b**, **4c**, **4e,** and **4g** exhibited high activity against both organisms in comparison with the antibiotic Nystatin.

Minimum inhibitory activity of fungal stain. The compounds **4c, 4e, 4f, and 4g** demonstrated the potent inhibitory activity at low concentrations against *Aspergillus niger* and *Aspergillus flavus* (Table 4), whereas the compounds **4a**, **4b** and **4d** did not show any antifungal activity in comparison with Nystatin.

EXPERIMENTAL

Melting points were determined in open capillary tubes. Purity of the compounds was tested by TLC on silica gel 60 F_{254} (Merck). Microwave assisted processes were carried out in a MultiSYNTH series microwave system (Milestone). IR spectra were recorded in KBr on a Perkin-Elmer 1800 spectrophotometer. ^{1}H NMR spectra were measured on a Varian VNMRS-400 spectrometer using TMS as an internal standard. Mass spectra were measured on a GCMS-QP 1000 mass spectrometer.

Synthesis of 4-oxo-4*H*-chromene-3-carbaldehydes (2a–2d). The Vilsmeier–Haack adduct was synthesized from $POCl_3$ (10 mmol) and *N*,*N*-dimethylformamide (25 mmol) at 0°C. A substituted-2-hydroxy acetophenone **1a–1d**, (1.0 mmol) was added to the Vilsmeier–Haack adduct and the mixture was stirred at room temperature for 16–18 h. Progress of the reaction was monitored by TLC. Upon completion of the process, the reaction mixture was poured into ice cold water and the white product was filtered off and dried. The products **2a–2d** were purified by recrystallization from petroleum ether : ethyl acetate mixture.

4-Oxo-4*H*-chromene-3-carbaldehyde (2a). Yield 85%, mp 148–150°C. IR spectrum, ν, cm^{-1}: 1694 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.49–7.55 m (2H), 7.74–7.78 m (1H), 8.30 d.d (1H, *J* = 8.0 Hz, 1.2 Hz), 8.55 s (1H), 10.36 s (1H); *M* 174 [*M* + H]$^+$. Found, %: C 68.91; H 3.52. $C_{10}H_6O_3$. Calculated, %: C 68.97; H 3.47.

6-Methyl-4-oxo-4*H*-chromene-3-carbaldehyde (2b). Yield 85%, mp 153–155°C. IR spectrum, ν, cm^{-1}: 1695 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.45 s (3H), 7.43 d (1H, *J* = 9.0 Hz), 7.56–7.58 m (1H), 8.10 s (1H), 8.52 s (1H), 10.38 s (1H). *M* 188.9 [*M* + H]$^+$. Found, %: C 70.25; H 4.32. $C_{11}H_8O_3$. Calculated, %: C 70.21; H 4.29.

6-Bromo-4-oxo-4*H*-chromene-3-carbaldehyde (2c). Yield 81%, mp 182–184°C. IR spectrum, ν, cm^{-1}: 1691 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.44 d (1H, *J* = 8.8 Hz), 7.84 d.d (1H, *J* = 1.2 Hz, 8.8 Hz), 8.42 s (1H), 8.54 s (1H), 10.36 s (1H). *M* 253 [*M* + H]$^+$. Found, %: C 47.40; H 2.02. $C_{10}H_5BrO_3$. Calculated, %: C 47.46; H 1.99.

6-Chloro-4-oxo-4*H*-chromene-3-carbaldehyde (2d). Yield 80%, mp172-174°C. IR spectrum, ν, cm^{-1}: 1694 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.51 d (1H, *J* = 8.8 Hz), 7.70 d.d (1H, *J* = 2.4 Hz, 8.8 Hz), 8.26 d (1H, *J* = 2.4 Hz), 8.54 s (1H), 10.37 s (1H). *M* 209 [*M* + H]$^+$. Found, %: C 57.53; H 2.41. $C_{10}H_5ClO_3$. Calculated, %: C 57.58; H 2.42.

Synthesis of (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones (3a–3g). *a. Conventional heating method.* A mixture of a substituted-2-hydroxy acetophenone **1a–1d** (10 mmol) with 4-oxo-4*H*-chromene-3-carbaldehydes **2a–2d** (10 mmol), and TEA (20 mmol) in ethanol was refluxed for 2.8–3.5 h. The process was monitored by TLC. Upon completion of the reaction, the mixture was poured into ice cold water. The product was extracted with EtOAc and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by column chromatography to afford pure (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones **3a–3g.**

b. Microwave irradiation method. A mixture of substituted-2-hydroxy acetophenones **1a–1d** (10 mmol) with 4-oxo-4*H*-chromene-3-carbaldehydes **2a–2d** (10 mmol), and TEA (20 mmol) in ethanol was subjected to microwave irradiation at 160 W for 4–5 min with intervals every 30 s. The process was monitored by TLC. Upon completion of the reaction the mixture was poured into ice cold water. The product was extracted with EtOAc and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by column chromatography to afford pure (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones **3a–3g.**

3-[(*E*)-3-(2-Hydroxyphenyl)-3-oxoprop-1-enyl]-4*H*-chromen-4-one (3a). IR spectrum, ν, cm^{-1}: 1637. ^{1}H NMR spectrum, δ, ppm: 7.05–7.01 m (2H), 7.60–7.55 m (2H), 7.76–7.68 m (2H), 7.89–7.85 m (1H), 7.97 d (1H, *J* = 6.8 Hz), 8.19–8.16 m (1H), 8.53 d (1H, *J* = 15.6 Hz), 9.07 s (1H), 12.27 s (1H). *M* 293 [*M* + H]$^+$. Found, %: C 73.92; H 4.10. $C_{18}H_{12}O_4$. Calculated, %: C 73.97; H 4.14.

3-[(*E*)-3-(2-Hydroxy-5-methylphenyl)-3-oxoprop-1-enyl]-4*H*-chromen-4-one (3b). IR spectrum, ν, cm^{-1}: 1640. ^{1}H NMR spectrum, δ, ppm: 2.33 s (3H), 6.92 d (1H, *J* = 8.8 Hz), 7.39 d (1H, *J* = 8.4 Hz), 7.58–7.60 t (1H, *J* = 7.6 Hz), 7.68–7.76 m (3H), 7.86–7.90 m (1H), 8.18 d (1H, *J* = 7.6 Hz), 8.51 d (1H, *J* = 15.2 Hz), 9.08 s (1H), 12.13 s (1H). *M* 307 [*M* + H]$^+$. Found, %: C 74.52; H 4.65. $C_{19}H_{14}O_4$. Calculated, %: C 74.50; H 4.61.

3-[(*E*)-3-(2-Hydroxy-5-methylphenyl)-3-oxoprop-1-enyl]-6-methyl-4*H*-chromen-4-one (3c). IR spectrum, ν, cm^{-1}: 1641. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H), 2.45 s (3H), 6.92 d (1H, *J* = 8.1 Hz), 7.31 d.d (1H, *J* = 2.1 Hz , 8.4 Hz), 7.42 d (1H, *J* = 8.4 Hz), 7.51–7.56 m

(2H), 7.81 s (1H), 8.10 s (1H), 8.21 s (1H), 8.79–8.84 d (1H, *J* = 15.3 Hz), 12.72 s (1H). *M* 321 $[M + H]^+$. Found, %: C 75.02; H 5.00. $C_{20}H_{16}O_4$. Calculated, %: C 74.99; H 5.03.

3-[(*E*)-3-(5-Bromo-2-hydroxyphenyl)-3-oxoprop-1-enyl]-4*H*-chromen-4-one (3d). IR spectrum, ν, cm^{-1}: 1637. ^1H NMR spectrum, δ, ppm: 6.99 d (1H, *J* = 8.4 Hz), 7.57–7.59 m (1H), 7.64–7.67 m (2H), 7.75 d (1H, *J* = 8.0 Hz), 7.85–7.87 m (1H), 7.96 s (1H), 8.17 d (1H, *J* = 8.0 Hz), 8.38 d (1H, *J* = 15.6 Hz), 9.08 s (1H), 11.86 s (1H). *M* 369 $[M - H]^-$. Found, %: C 58.29; H 3.03. $C_{18}H_{11}BrO_4$. Calculated, %: C 58.24; H 2.99.

6-Bromo-3-[(*E*)-3-(5-bromo-2-hydroxyphenyl)-3-oxoprop-1-enyl]-4*H*-chromen-4-one (3e). IR spectrum, ν, cm^{-1}: 1642. ^1H NMR spectrum, δ, ppm: 7.54 d.d (1H, *J* = 2.8 Hz , 9.2 Hz), 7.60 d (1H, *J* = 15.2 Hz), 7.60 d (1H, *J* = 8.8 Hz), 7.82–7.78 m (2H), 7.80 d.d (1H, *J* = 2.4 Hz, 8.6 Hz), 8.04 d (1H, *J* = 2.4 Hz), 8.35 d (1H, *J* = 15.2 Hz), 9.09 s (1H), 11.75 s (1H). *M* 449 $[M + H]^+$. Found, %: C 48.05; H 2.28. $C_{18}H_{10}BrO_4$. Calculated, %: C 48.03; H 2.24.

3-[(*E*)-3-(5-Chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl]-4*H*-chromen-4-one (3f). IR spectrum, ν, cm^{-1}: 1639. ^1H NMR spectrum, δ, ppm: 7.05 d (1H, *J* = 8.8 Hz), 7.59–7.55 m (2H), 7.66 d (1H, *J* = 15.6 Hz), 7.75 d (1H, *J* = 8.0 Hz), 7.84–7.89 m (2H), 8.17 d.d (1H, *J* = 1.2 Hz, 7.6 Hz), 8.39 d (1H, *J* = 15.6 Hz), 9.08 s (1H), 11.85 s (1H). *M* 325 $[M - H]^-$. Found, %: C 66.11; H 3.45. $C_{18}H_{11}ClO_4$. Calculated, %: C 66.17; H 3.39.

6-Chloro-3-[(*E*)-3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl]-4*H*-chromen-4-one (3g). IR spectrum, ν, cm^{-1}: 1652. ^1H NMR spectrum, δ, ppm:, 7.04 d (1H, *J* = 8.8 Hz) 7.56 d.d (1H, *J* = 2.4 Hz, 8.8 Hz), 7.63 d (1H, *J* = 15.6 Hz), 7.81–7.84 m (2H), 7.91 d.d (1H, *J* = 2.4 Hz , 8.8 Hz), 8.09 d (1H, *J* = 2.4 Hz), 8.37 d (1H, *J* = 15.6 Hz), 9.10 s (1H), 11.78 s (1H). *M* 359 $[M - H]^-$. Found, %: C 59.88; H 2.83. $C_{18}H_{10}Cl_2O_3$. Calculated, %: C 59.86; H 2.79.

Synthesis of 3-{(*Z*)-[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-ones (4a–4g). *Method 1. Using $Hg(OAc)_2$ in pyridine.* Mercury (II) acetate (1 mmol) was dissolved in pyridine (10 mL) upon cooling and to this solution a (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones **3a–3g** (1 mmol) was added. The mixture was refluxed for 5 h. Upon completion of the process (TLC), the reaction mixture was cooled down to room temperature and then poured into ice cold water and acidified by 2 M hydrochloric acid solution. The precipitated product was filtered off, washed with ice cold water, dried, and crystallized from EtOH to gave 3-{(*Z*)-[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-ones **4a–4g**.

Method 2. Using $CuBr_2$ in DMSO. $CuBr_2$ (2 mmol) and (*E*)-3-[3-(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]-4*H*-chromen-4-ones **3a–3g** (1 mmol) were added to DMSO (10 mL). The reaction mixture was heated at 90°C for 2 h. Upon completion of the process (TLC), the reaction mixture was cooled down to room temperature and then poured into ice cold water and stirred for 10–15 min. The precipitated material was filtered off, washed with ice cold water, dried, and crystallized from EtOH gave 3-{(*Z*)-[3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-ones **4a–4g**.

3-{(*Z*)-[3-Oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one (4a). IR spectrum, ν, cm^{-1}: 1702. ^1H NMR spectrum, δ, ppm: 7.27 s (1H), 7.31 d (1H, *J* = 8.4 Hz), 7.37 s (1H), 7.44–7.53 m (2H), 7.65–7.74 m (2H), 7.82 d (1H, *J* = 7.2 Hz), 8.31 d (1H, *J* = 8.0 Hz), 9.08 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 102.2, 112.7, 118.1, 118.2, 121.7, 123.6, 123.8, 124.8, 125.8, 126.5, 134.1, 136.9, 147.2, 155.9, 158.8, 165.5, 175.1, 183.6. *M* 291 $[M + H]^+$. Found, %: C 73.92; H 4.10. $C_{18}H_{10}O_4$. Calculated, %: C 73.97; H 4.14.

3-{(*Z*)-[5-Methyl-3-oxobenzofuran-2(3*H*)-ylidene]-methyl}-4*H*-chromen-4-one (4b). IR spectrum, ν, cm^{-1}: 1704. ^1H NMR spectrum, δ, ppm: 2.38 s (3H), 6.99 s (1H), 7.46 (1H, d, *J* = 8.4 Hz), 7.55–7.66 m (3H), 7.75 d (1H, *J* = 8.4 Hz), 7.89 t (1H, *J* = 7.6 Hz), 8.16 d (1H, *J* = 8.0 Hz), 9.23 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 21.0, 102.0, 112.7, 118.1, 118.2, 120.1, 123.8, 124.6, 125.3, 125.8, 126.5, 134.1, 147.2, 149.2, 155.9, 158.7, 165.9, 175.2, 183.3. *M* 305 $[M + H]^+$. Found, %: C 74.94; H 3.99. $C_{19}H_{12}O_4$. Calculated, %: C 74.99; H 3.97.

6-Methyl-3-{(*Z*)-[5-methyl-3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one (4c). IR spectrum, ν, cm^{-1}: 1707. ^1H NMR spectrum, δ, ppm: 2.38 s (3H), 2.45 s (3H), 7.00 s (1H), 7.45 d (1H, *J* = 8.4 Hz), 7.57–7.71 m (4H), 7.95 s (1H), 9.21 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 20.7, 20.9, 102.1, 112.3, 117.9, 118.0, 122.8, 125.1, 125.8, 126.8, 131.4, 135.3, 137.1, 137.9, 147.4, 148.7, 153.2, 158.7, 164.0, 176.6, 182.8. *M* 319 $[M + H]^+$. Found, %: C 75.44; H 4.44. $C_{20}H_{14}O_4$. Calculated, %: C 75.46; H 4.43.

3-{(*Z*)-[5-Bromo-3-oxobenzofuran-2(3*H*)-ylidene]-methyl}-4*H*-chromen-4-one (4d). IR spectrum, ν, cm^{-1}:

1707. ^{1}H NMR spectrum, δ, ppm: 7.05 s (1H), 7.56–7.60 m (2H), 7.76 d (1H, *J* = 8.4 Hz), 7.90 t (1H, *J* = 8.0 Hz), 7.98–8.00 m (2H), 8.17 d (1H, *J* = 8.0 Hz), 9.28 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 103.2, 113.9, 118.1, 124.3, 125.6, 126.9, 128.9, 135.0, 136.1, 147.7, 155.6, 158.7, 165.1, 174.9, 182.5. *M* 369 $[M + H]^+$. Found, %: C 59.61; H 2.93. $C_{18}H_9BrO_4$. Calculated, %: C 59.55; H 2.89.

6-Bromo-3-{(*Z*)-[5-bromo-3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one (4e). IR spectrum, ν, cm^{-1}: 1709. ^{1}H NMR spectrum, δ, ppm: 7.14 s (1H), 7.72–7.78 m (3H), 7.87 d (1H, *J* = 2.4 Hz), 8.03 d.d (1H, *J* = 2.8 Hz , 9.2 Hz), 8.18 d (1H, *J* = 2.4 Hz), 9.25 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 101.9, 112.3, 119.0, 120.4, 121.0, 121.9, 123.5, 123.6, 124.8, 125.7, 131.0, 134.2, 136.4, 147.3, 155.9, 156.8, 164.5, 174.6, 183.2. *M* 447 $[M + H]^+$. Found, %: C 48.28; H 1.83. $C_{18}H_8BrO_4$. Calculated, %: C 48.25; H 1.80.

3-{(*Z*)-[5-Chloro-3-oxobenzofuran-2(3*H*)-ylidene]-methyl}-4*H*-chromen-4-one (4f). IR spectrum, ν, cm^{-1}: 1704. ^{1}H NMR spectrum, δ, ppm: 7.06 s (1H), 7.60–7.62 m (2H), 7.74 d (1H, *J* = 8.0 Hz), 7.92 t (1H, *J* = 8.2 Hz), 7.98–8.10 m (2H), 8.16 d (1H, *J* = 7.8 Hz), 9.26 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 103.5, 114.1, 118.3, 124.5, 125.9, 126.6, 129.6, 134.3, 136.7, 147.2, 155.9, 158.9, 164.2, 175.0, 182.3. *M* 325 $[M + H]^+$. Found, %: C 66.62; H 2.83. $C_{18}H_9ClO_4$. Calculated, %: C 66.58; H 2.79.

6-Chloro-3-{(*Z*)-[5-chloro-3-oxobenzofuran-2(3*H*)-ylidene]methyl}-4*H*-chromen-4-one (4g). IR spectrum, ν, cm^{-1}: 1710. ^{1}H NMR spectrum, δ, ppm: 7.01 s (1H), 7.62 d (1H, *J* = 8.8 Hz), 7.84–7.90 m (3H), 7.94 d.d (1H, *J* = 2.4 Hz , 9.2 Hz), 8.10 d (1H, *J* = 2.8 Hz), 9.29 s (1H). ^{13}C NMR spectrum, δ_C, ppm: 102.8, 112.5, 118.5, 120.3, 120.5, 121.0, 123.6, 123.7, 124.5, 124.6, 125.9, 131.6, 134.5, 136.8, 147.5, 156.2, 157.4, 164.7, 174.7, 183.4. *M* 359 $[M + H]^+$. Found, %: C 60.22; H 2.31. $C_{18}H_8Cl_2O_3$. Calculated, %: C 60.19; H 2.25.

Antibacterial activity. Synthesized compounds have been assayed for their antimicrobial activity. The entire organisms were collected from Department of Microbiology, Osmania University, Hyderabad. Seven bacterial strains *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 15380, *Pseudomonas aeruginosa* ATCC 12454, *Staphylococcus aureus* ATCC 25923, and *Streptococcus pyogenes* ATCC 35552 were used in the study. Microbial cultures were stored at –20°C in micro-centrifuge tubes having 40% sterile glycerol. The synthesized compounds inhibitory activity was tested according to the "well plate or disc diffusion method" [15, 16]. The minimum inhibitory concentration was determined using the tube dilution techniques [15, 16]. Various concentrations of each compound were prepared using single dilution method. The least concentration of each compound that did not permit any visible growth or turbidity of the inoculated test organisms in broth culture was taken as the minimum inhibitory concentration in each case.

Antifungal activity. Antifungal activity was studied by the well plate or disc diffusion method [17, 18]. The MIC was determined by the broth micro dilution method using 96-well micro-plates [17, 18]. Each sample (1.0 mg) was dissolved in DMSO (1 mL) to obtain 1000 μg/mL stock solution. Nystatin was used as a positive control. Plates were incubated at 37°C for 24 h.

CONCLUSIONS

A series of aurones have been synthesized and tested for their antibacterial and antifungal activities. The aurones were synthesized using $Hg(OAc)_2$ and $CuBr_2$. The former led to higher yields of the products. Positions of the substituents and their electronic nature seem to play an important role in biological activity of the synthesised compounds. The compounds **4c** and **4e** are more potent and the compound **4g** is moderately potent for pathogenic bacteria and fungi compared to the standard drugs.

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