Med Chem Res (2015) 24:1487–1495
DOI 10.1007/s00044-014-1204-9

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

# Microwave-assisted synthesis of substituted 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-ones and their antimicrobial activity

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Received: 9 May 2014 / Accepted: 6 July 2014 / Published online: 24 August 2014


**Abstract** Chromene and coumarin scaffolds are known for their potential antimicrobial activity. Herein, we have synthesized hybrid compounds containing both, substituted 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-ones, **3a–o** have been synthesized from substituted (*E*)-1-(7-Hydroxy-4-methyl-8-coumarinyl)-3-phenyl-2-propen-1-ones, **2a–o** in good yield using the microwave-assisted Vilsmeier–Haack reaction. All the synthesized compounds were tested in vitro for their antimicrobial activity. The compounds **3e**, **3f** and **3g** were found to be potent against tested fungal and bacterial strains.

**Keywords** Antimicrobial activity · Chromene · Coumarin · Microwave irradiation · Vilsmeier–Haack reagent

## Introduction

Chromenes have been widely employed as important intermediates in the synthesis of many natural products and medical agents. They are widely distributed in nature displaying diverse range of biological activities (Cassidy *et al.*, 1992). These are found to be interesting sharing common structural features for a family of potassium channel activating drugs (Ashwood *et al.*, 1986). They also serve as the framework of tannins (Rochfort *et al.*, 1996), which are becoming important because of their health-promoting effects found in red wine, vegetables, fruits and teas.

4-Chlorochromene derivatives are extensively used as versatile building blocks for the synthesis of many oxygen heterocyclic systems with potential biological activity (Rimbault *et al.*, 1985).

Chromenes and fused chromenes have raised the interest of researchers because of their potential for different biological activities including antibacterial (El-Agrody *et al.*, 2000, Zamocka *et al.*, 1992), antifungal (Ohira and Yatagai, 1993) antitumor (Mohr *et al.*, 1975), and antiviral (Martinez and Marco, 1997) activities. Coumarin derivatives have been reported to exhibit anti-inflammatory (Jung *et al.*, 2008), antimicrobial (Mulwad and Shirodkhar, 2002), antioxidant (Kusanur *et al.*, 2004), anticancer (Musiliyu *et al.*, 2011) and chemoprophylactic (Nofal *et al.*, 2005) activities. The pyranocoumarins *soulattrolide*, *inophyllum G-1*, *cordatolide A* and *oblongulide* are found to exhibit potential anti-HIV activity (Patil *et al.*, 1993). Herein we hypothesized that hybrid compounds containing both coumarin and chromene moieties, called pyranocoumarins may exhibit better biological activity.

In recent years, microwave-assisted organic synthesis (MAOS) has gained popularity as an environmental benign technology. Microwave-assisted synthesis leads to significant reduced reaction times, enhanced conversions and known to be environment friendly. Earlier, we have reported 4-chlorochromene derivatives possessing potential antimicrobial activity (Ashok *et al.*, 2012). Encouraged by the pharmacological activities of chlorochromenes, chromenes and fused chromenes, we wish to report some new 4-Chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-ones by simple and convenient microwave irradiation method. Here, we described the synthesis of some

**Electronic supplementary material** The online version of this article (doi:10.1007/s00044-014-1204-9) contains supplementary material, which is available to authorized users.

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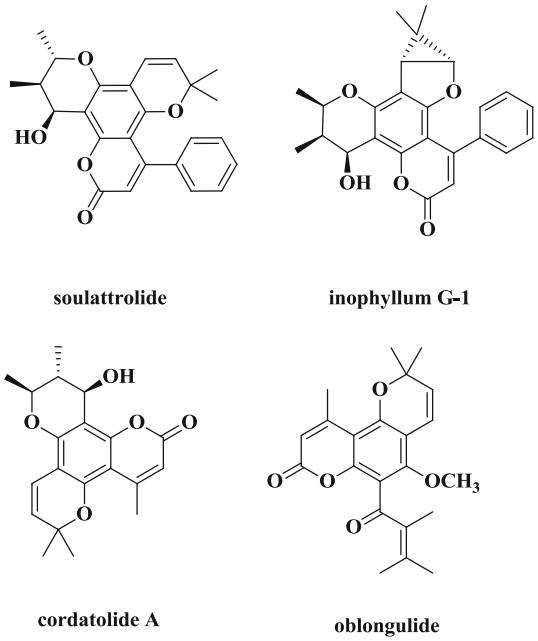


**Fig. 1** Representative examples of pyranocoumarin derivatives, exhibiting anti-HIV activity

new pyranocoumarin derivatives (**3a–o**) from 8-acetyl-7-hydroxy-4-methyl-2*H*-chromen-2-one **1** and their antimicrobial activity (Fig. 1).

## Results and discussion

### Chemistry

The synthetic route to compounds **3a–o** was shown in Scheme 1. Compounds **2a–o** were synthesized according to the literatures (Khan and Sharma, 1993). The condensation of 8-acetyl-7-hydroxy-4-methyl coumarin **1** with aromatic or hetero aromatic aldehydes in the presence of piperdine under microwave irradiation gave substituted (*E*)-1-(7-hydroxy-4-methyl-8-coumarinyl)-3-phenyl-2-propen-1-ones **2a–o** in excellent yields. Subsequently, these chalcones **2a–o** on reaction with Vilsmeier–Haack reagent ($DMF/POCl_3$) yielded substituted 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-ones **3a–o**. Initially, we performed the reaction at room temperature but there was no product formed. Optimum results were obtained when the temperature was maintained at 90–100 °C by using 6 equivalents of $POCl_3$.

In case of microwave irradiation method, optimum results obtained by irradiating at 160 W for 4–5 min. The crude product was purified using column chromatography to afford pure product.

The yields obtained with microwave irradiation were better than conventional heating method (Table 1). Microwave irradiations are known to be useful for variety of organic reactions due to short reaction time, cleaner reactions, easier work-up and good yield.

### *Spectroscopic characterisation*

Compound **3a** was characterized as 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-one by using spectral data.

*IR characterisation* In the IR spectrum, **3a** showed a peak due to the C–O–C group at 1,082 $cm^{-1}$. The peak at 1,732 $cm^{-1}$ is due to the C–O stretching of carbonyl group.

*$^1H$ NMR characterisation* In $^1H$ NMR spectrum, the methyl protons attached to $C_8$ appeared as a doublet at δ 2.41 ppm. The protons, $H_2$, $H_3$, $H_7$ and $H_9$ appeared as doublets at δ 5.87 ppm, δ 6.15 ppm, δ 6.21 ppm and δ 6.89 ppm, respectively. The multiplet at δ 7.39–7.50 ppm with proton integration 6 is due to aromatic protons and $H_{10}$.

*$^{13}C$ NMR characterisation* In $^{13}C$ NMR spectrum, peak corresponding to methyl carbon appeared at δ 18.9 ppm. The peak at δ 77.9 ppm corresponding to $C_2$ confirms the formation of 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-one.

*Mass spectral data* In the MS of **3a**, the base peak appeared at 325 corresponding to $(M + H)^+$.

**Scheme 1** Synthesis of substituted 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2*H*-phenanthren-6-ones

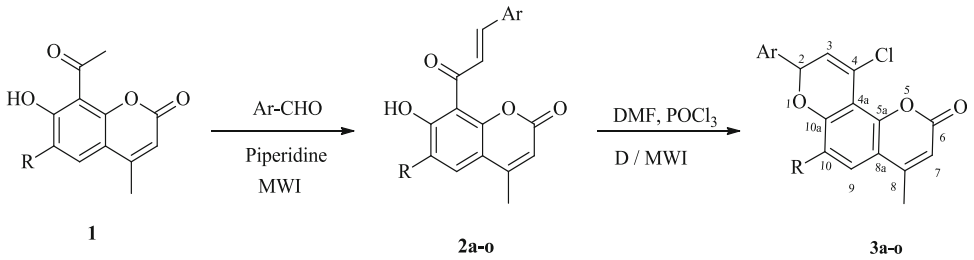

**Table 1** Physical data of synthesized compounds **3a–o**

| Compound | R | Ar | M.P. (°C) | Conventional heating | | Microwave irradiation | |
|---|---|---|---|---|---|---|---|
| | | | | Time (h) | Yield (%) | Time (min) | Yield (%) |
| **3a** | H | Phenyl | 158–160 | 5 | 68 | 4 | 80 |
| **3b** | Cl | Phenyl | 154–156 | 5 | 70 | 4 | 83 |
| **3c** | H | 4-Methoxyphenyl | 176–178 | 6 | 70 | 5 | 83 |
| **3d** | Cl | 4-Methoxyphenyl | 170–172 | 6 | 69 | 5 | 83 |
| **3e** | H | 3,4-Dimethoxyphenyl | 160–162 | 5.5 | 65 | 5 | 80 |
| **3f** | Cl | 3,4-Dimethoxyphenyl | 158–160 | 5.5 | 70 | 5 | 85 |
| **3g** | H | 4-Fluorophenyl | 175–177 | 6 | 70 | 5 | 84 |
| **3h** | Cl | 4-Fluorophenyl | 172–174 | 6 | 68 | 5 | 80 |
| **3i** | H | 4-Methylphenyl | 142–144 | 5 | 65 | 4 | 80 |
| **3j** | Cl | 4-Methylphenyl | 139–141 | 5 | 70 | 4 | 84 |
| **3k** | H | 2-Chlorophenyl | 156–158 | 5 | 65 | 4 | 82 |
| **3l** | Cl | 2-Chlorophenyl | 154–156 | 5 | 60 | 4 | 80 |
| **3m** | H | 1-Naphthyl | 136–138 | 5.5 | 62 | 5 | 80 |
| **3n** | Cl | 1-Naphthyl | 133–135 | 5.5 | 65 | 5 | 80 |
| **3o** | H | 2-Thienyl | 155–157 | 5 | 70 | 4 | 85 |

## Microbiology

### Antibacterial activity

The synthesized novel compounds (**3a–o**) were screened for antibacterial activity against different types of bacterial strains viz. Gram-positive bacterial strains *Bacillus subtillis* and *Staphylococcus aeureus*; Gram-negative bacterial strains *Klebsiella pneumoniae* and *Escherichia coli* at a concentration of 10 and 20 μg/mL.

Some of the synthesized compounds have shown potent activity and some compounds have shown moderate activity compared to standard drug *Gatifloxacin* at a concentration of 10 and 20 μg/mL.

The compound **3e** (R=H, Ar=3,4-dimethoxyphenyl), **3f** (R=Cl, Ar=3,4,-dimethoxyphenyl) and **3o** (R=H, Ar=2-thienyl) shown potent activity with zone of inhibition (Table 2) against *Staphylococcus aeureus*, *Bacillus subtilis*, *Escherichia coli* and *Klebsiella pneumoniae* respectively compared to the standard drug at a concentration of 10 and 20 μg/mL. The compounds **3d** (R=Cl, Ar=4-methoxyphenyl), **3k** (R=H, Ar=2-chlorophenyl) and **3l** (R=Cl, Ar=2-chlorophenyl) have shown similar activity profile compared to the standard drug at a concentration of 10 and 20 μg/mL. All other compounds have shown moderate activity compared to standard.

### Antifungal activity

The antifungal activity of synthesized compounds **3a–o** were tested against three pathogenic fungi viz. *Fusarium oxysporum, Aspergillus nigerzeae,* and *Aspergilus flavus*, by the poison plate technique at a concentration of 100 μg/mL (Song *et al.*, 2004). Some synthesized compounds shown moderate to high antifungal activity compared to standard drug Clotrimazole at a concentration of 100 μg/mL. Compound **3e** (R=H, Ar=3,4-dimethoxyphenyl), **3o** (R=H, Ar=2-thienyl) have shown better activity than standard drug against *Aspergillus nigerzeae, Aspergilus flavus* and *Fusarium oxysporum*. The compound **3f** (R=Cl, Ar=3,4-dimethoxyphenyl) and **3j** (R=Cl, Ar=4-methylphenyl) have shown similar activity compared to standard drug against tested fungi where as the remaining compounds shown moderate activity against pathogenic fungi, compared to standard (Figs. 2, 3).

## Experimental

### Materials

Melting points were determined in open capillaries and are uncorrected. Purity of the compounds was checked by TLC on silica gel 60 $F_{254}$ (Merck). Microwave reactions were carried out in a multi SYNTH series microwavw system (Milestone).

### SYNTH series microwave system (Milestone)

$^{1}$H NMR and $^{13}$C NMR spectra were recorded on Bruker Avance II 400 spectrometer using TMS as an internal standard. IR spectra were recorded in KBr on a Shimadzu FTIR 8400S spectrophotometer. Mass spectra were recorded on a GCMS-QP 1000 mass spectrometer (Fig. 4).

**Table 2** Antibacterial activity of compounds **3a–o** at different concentrations 20 and 20 μg/mL

| Compound | Zone of inhibition (mm) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Gram positive bacteria | | | | Gram negative bacteria | | | |
| | *Stapylococus aeureus* | | *Bacillus subtilis* | | *Escherichia coli* | | *Klebsiella pneumonia* | |
| | 10 μg/mL | 20 μg/mL | 10 μg/mL | 20 μg/mL | 10 μg/mL | 20 μg/mL | 10 μg/mL | 20 μg/mL |
| **3a** | 13 | 35 | 18 | 31 | 07 | 08 | 04 | 10 |
| **3b** | 15 | 36 | 20 | 33 | 10 | 10 | 06 | 14 |
| **3c** | 16 | 34 | 24 | 22 | 14 | 22 | 06 | 14 |
| **3d** | 17 | 35 | 29 | 28 | 15 | 24 | 08 | 18 |
| **3e** | 28 | 33 | 24 | 43 | 17 | 21 | 11 | 20 |
| **3f** | 30 | 36 | 28 | 48 | 20 | 26 | 13 | 25 |
| **3g** | 15 | 15 | 18 | 28 | 07 | 18 | 10 | 10 |
| **3h** | 18 | 22 | 16 | 32 | 10 | 20 | 10 | 15 |
| **3i** | 12 | 14 | 16 | 25 | 15 | 12 | 06 | 12 |
| **3j** | 15 | 18 | 18 | 27 | 17 | 22 | 08 | 15 |
| **3k** | 20 | 28 | 20 | 35 | 12 | 17 | 08 | 12 |
| **3l** | 21 | 30 | 22 | 42 | 14 | 20 | 10 | 18 |
| **3m** | 24 | 28 | 12 | 29 | 09 | 18 | 05 | 13 |
| **3n** | 14 | 30 | 16 | 35 | 12 | 20 | 10 | 16 |
| **3o** | 22 | 36 | 28 | 48 | 17 | 21 | 15 | 20 |
| *Gatifloxacin* | 20 | 30 | 20 | 40 | 15 | 20 | 10 | 18 |

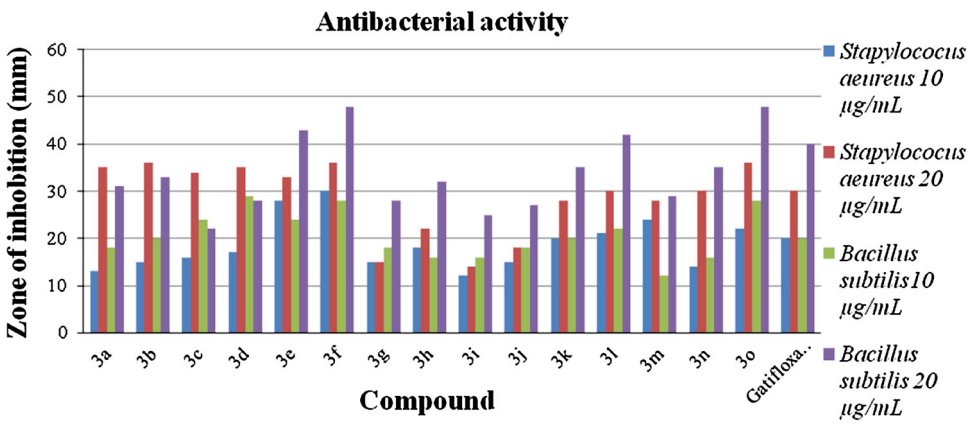


**Fig. 2** Antibacterial activity against gram-positive bacterial strains

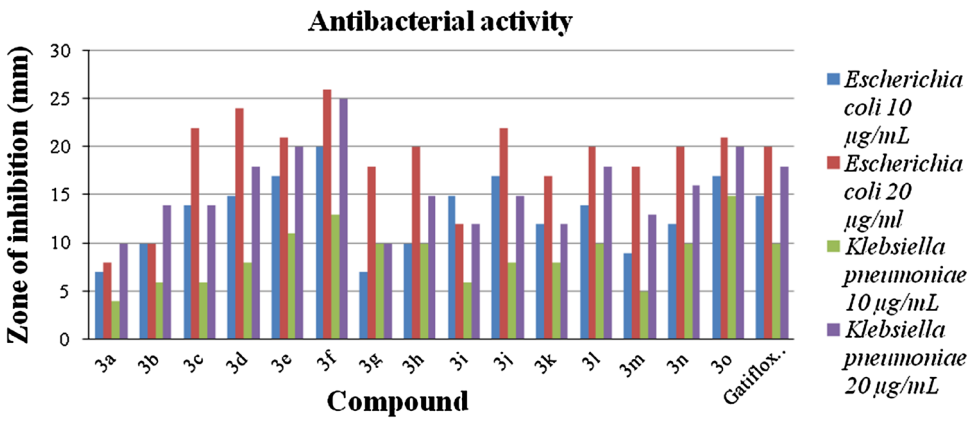


**Fig. 3** Antibacterial activity against gram-negative bacterial strains

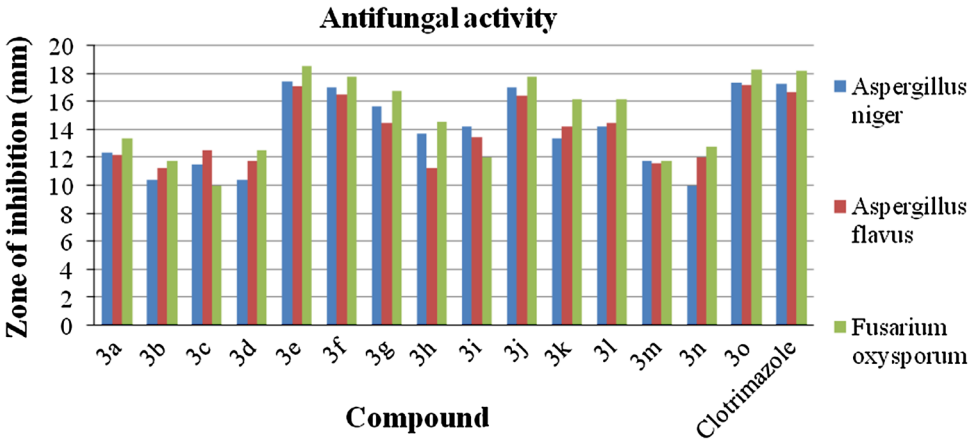


**Fig. 4** Antifungal activity

## Biological assay

### Antibacterial activity

The synthesized novel compounds **3a–o** were screened for their Antibacterial activity against different types of bacterial strains, they are Gram-negative bacterial strains of *Klebsiella pneumoniae and Escherichia coli*, Gram-positive bacterial strains of *Bacillus subtilis and Staphylococcus aeureus* at a concentration of 10 and 20 μg/mL .

The cultures were diluted with 5 % saline autoclaved and the final volume was made with concentration approximately $10^5$–$10^6$ CFU/mL. The synthesized compounds were diluted in acetone for antibacterial biological assays. For agar disc diffusion method (Benson *et al.*, 1990), the liquid form of test compound was soaked on to the disc and then allowed to air dry, such that the disc gets completely saturated with test compound. The saturated chemical discs were introduced onto the upper layer of the medium evenly flooded with the bacteria.

The discs were dipped in different chemical samples, were placed over the evenly spread bacterial nutrient media, and incubated at 37 °C for 24–48 h for better inhibition of bacteria. The zones of inhibition were measured after 24–48 h. All the experiments were carried out in triplicates and the results were expressed as zone of Inhibition in mm. The zones of inhibition of synthesized compounds **3a–o** were compared with the zone of inhibition of standard antibiotic concentrations of gatifloxacin (10, 20 μg/mL). The Antibacterial activity was evaluated and the results are presented in Table 2.

### Antifungal activity

The antifungal activity of synthesized compounds **3a–o** was tested against three pathogenic fungi, namely *Fusarium oxysporum, Aspergillus niger,* and *Aspergilus flavus*, by the poison plate technique at a concentration of 100 μg/mL. Three kinds of fungi were incubated in PDA at 25 ± 1 °C for 5 days to get new mycelium for antifungal assay, then a mycelia as discs of approximately 0.45 cm diameter cut from the culture medium were picked up with a sterilised inoculation needle and inoculated in the center of PDA plate. Test compounds were dissolved in acetone (10 mL) then added to the Potato Dextrose Agar medium (PDA, 90 mL). The final concentration of compounds in the medium was adjusted to 100 μg/mL. The inoculated plates were incubated at 25 ± 1 °C for 5 days. Acetone was diluted with sterilised distilled water and used as control, while clotrimazole (100 μg/mL) was used as standard control for each treatment three replicates of experiments were carried out. The radial growth of the fungal colonies was measured on the 6th day. The Antifungal activity was evaluated and the results are presented in Table 3.

**Table 3** Antifungal activity of the compounds **3a–o**

| Compound | Zone of inhibition (mm) | | |
|---|---|---|---|
| | *Aspergillus niger* | *Aspergillus flavus* | *Fusarium oxysporum* |
| **3a** | 12.4 | 12.2 | 13.4 |
| **3b** | 10.4 | 11.3 | 11.8 |
| **3c** | 11.5 | 12.5 | 10.0 |
| **3d** | 10.4 | 11.8 | 12.5 |
| **3e** | 17.5 | 17.1 | 18.6 |
| **3f** | 17.0 | 16.5 | 17.8 |
| **3g** | 15.7 | 14.5 | 16.8 |
| **3h** | 13.7 | 11.3 | 14.6 |
| **3i** | 14.2 | 13.5 | 12.0 |
| **3j** | 17.0 | 16.4 | 17.8 |
| **3k** | 13.4 | 14.2 | 16.2 |
| **3l** | 14.2 | 14.5 | 16.2 |
| **3m** | 11.8 | 11.6 | 11.8 |
| **3n** | 10.0 | 12.0 | 12.8 |
| **3o** | 17.4 | 17.2 | 18.3 |
| Clotrimazole | 17.3 | 16.7 | 18.2 |

General procedures

*Synthesis of compounds 10-chloro-4-methyl-8-aryl-2H,8H-pyrano[2,3-f] Chromen-2-ones(**3a–3o**) under conventional conditions*

DMF (5 mL) was taken into round bottomed flask and it was cooled to 0–5 °C. $POCl_3$ (0.006 mol) was added drop wise to it under stirring. It was stirred at 0–5 °C for 15 min and then substituted (*E*)-1-(7-Hydroxy-4-methyl-8-coumarinyl)-3-phenyl-2-propen-1-ones **2a–o** (0.001 mol) solution in 3 mL of DMF was added to it at 0–5 °C. It was maintained at 0–5 °C for 30 min. The reaction mixture was heated in water bath for 6–8 h. After the completion of the reaction (monitored by TLC, EtOAc:Hexane, 1:3 v/v), the reaction mixture was poured into ice–water and neutralised with 10 % NaOH solution, and it was extracted with Chloroform (2 × 20 mL); the combined organic layer was washed with 10 mL water and was dried over anhydrous magnesium sulphate. The solvent was evaporated and the residue was purified by using silica gel column chromatography to afford pure product **3a–o**.

*Synthesis of compounds 4-chloro-8-methyl-2-phenyl-1,5-dioxa-2H-phenanthren-6-ones (**3a–3o**) under microwave irradiation*

DMF (5 mL) was taken into round bottomed flask and it was cooled to 0–5 °C. $POCl_3$ (0.006 mol) was added drop wise to it under stirring. It was stirred at 0-5 °C for 15 min and then substituted (*E*)-1-(7-hydroxy-4-methyl-8-coumarinyl)-3-phenyl-2-propen-1-ones **2a–o** (0.001 mol) solution in 3 mL of DMF was added to it at 0–5 °C. It was maintained at 0–5 °C for 30 min. The reaction mixture was placed in the microwave oven and subjected to microwave irradiation at 160 W for 4–5 min. The progress of reaction was monitored by TLC (EtOAc: Hexane, 1:4 v/v). After the completion of the reaction, it was poured into ice-water and neutralised with 10 % NaOH solution and extracted with chloroform (2 × 20 mL) and the combined organic layer was washed with 10 mL water, and it was dried over anhydrous magnesium sulphate. The solvent was evaporated and the residue was purified by using silica gel column chromatography to afford pure product **3a–o**.

*4-Chloro-8-methyl-2-phenyl-1,5-dioxa-2H-phenanthren-6-one (**3a**)* Colourless solid, yield = 80 %, mp 158–160 °C; IR (KBr) ($cm^{-1}$): 1082 (C–O–C), 1732 (C=O); $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.41 (d, 3H, =C–$CH_3$, $J$ = 1.0 Hz), 5.87 (d, 1H, $H_2$, $J$ = 4.5 Hz), 6.15 (d, 1H, $H_3$, $J$ = 4.5 Hz), 6.21 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.89 (d, 1H, $H_9$, $J$ = 8.7 Hz) 7.39–7.50 (m, 6H, $H_{10}$, Ar–H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 77.9 (C-2), 111.1 (C-4a), 113.4 (C-8a), 115.2 (C-7), 118.4 (C-10), 125.1 (C-9), 125.5 (C-3), 126.2 (C, Ar–C), 127.0 (C, Ar–C), 128.7 (2C, Ar–C), 129.1 (2C, Ar–C), 137.3 (C-4), 148.6 (C-5a), 151.4 (C-8) 152.6 (C-10a), 159.3 (C-6). MS (*m/z*): 325 $(M + H)^+$ (100 %). Anal. Calcd. for $C_{19}H_{13}ClO_3$: C, 70.27; H, 4.03. Found: C, 70.24; H, 3.99.

*4,10-Dichloro-8-methyl-2-phenyl-1,5-dioxa-2H-phenanthren-6-one (**3b**)* Colourless solid, yield = 83 %, mp 154–156 °C; IR (KBr) ($cm^{-1}$): 1084 (C–O–C), 1734 (C=O); $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.36 (d, 3H, =C–$CH_3$, $J$ = 1.0 Hz), 5.98 (d, 1H, $H_2$, $J$ = 4.7 Hz), 6.21 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.26 (d, 1H, $H_3$, $J$ = 4.7 Hz), 7.34–7.52 (m, 6H, $H_9$, Ar–H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 77.9 (C-2), 111.1 (C-4a), 113.4 (C-8a), 115.2 (C-7), 118.4 (C-10), 125.1 (C-9), 125.5(C-3), 126.2 (C, Ar–C), 127.0 (C, Ar–C), 128.7 (2C, Ar–C), 129.1 (2C, Ar–C), 137.3 (C-4), 148.6 (C-5a), 151.4(C-8) 152.6 (C-10a), 159.3 (C-6). MS (*m/z*): 358 ($M^+$) (100 %). Anal. Calcd. for $C_{19}H_{12}Cl_2O_3$: C, 63.53; H, 3.37. Found: C, 63. 50; H, 3.34.

*4-Chloro-2-(4-methoxyphenyl)-8-methyl-1,5-dioxa-2H-phenanthren-6-one (**3c**)* Colourless solid, yield = 83 %, mp 176–178 °C; IR (KBr) ($cm^{-1}$): 1088 (C–O–C), 1725 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, =C-$CH_3$, $J$ = 1.2 Hz), 3.80 (s, 3H,-$OCH_3$) 5.79 (d, 1H, $H_2$, $J$ = 4.2 Hz), 6.11 (d, 1H, $H_3$, $J$ = 4.2 Hz), 6.18 (d, 1H, $H_7$, $J$ = 1.2 Hz), 6.83 (d, 1H, $H_{10}$, $J$ = 8.4 Hz), 6.89 (d, 2H, Ar–H, $J$ = 8.1 Hz), 7.37 (d, 2H, Ar–H, $J$ = 8.1 Hz), 7.44 (d, 1H, H9, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 19.0 ($CH_3$), 55.3 ($OCH_3$), 76.4 (C-2), 109.6 (C-4a), 112.3 (C-8a), 113.3 (C-7), 114.1 (C-10), 114.9 (2C–Ar), 124.6 (C-9), 125.5 (C-3), 126.4 (C–Ar), 129.0 (C-4), 129.8 (2C-Ar), 150.2 (C–Ar), 152.3 (C-5a), 157.3 (C-8), 160.0 (C-10a), 160.2 (C-6). MS (*m/z*): 355 $(M + H)^+$ (100 %). Anal. Calcd. for $C_{20}H_{15}ClO_4$: C, 67.71; H, 4.26. Found: C, 67.67; H, 4.21.

*4,10-Dichloro-2-(4-methoxyphenyl)-8-methyl-1,5-dioxa-2H-phenanthren-6-one (**3d**)* Colourless solid, yield = 83 %, mp 170–172 °C; IR (KBr) ($cm^{-1}$): 1088 (C–O–C), 1730 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.36 (d, 3H, = C-$CH_3$, $J$ = 1.2 Hz), 3.81 (s, 3H, –$OCH_3$) 5.99 (d, 1H, $H_2$, $J$ = 4.2 Hz), 6.21 (d, 1H, $H_7$, $J$ = 1.2 Hz), 6.26 (d, 1H, $H_3$, $J$ = 4.2 Hz), 7.34–7.48 (m, 4H, Ar–H), 7.52 (s, 1H, $H_9$); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 55.8 ($OCH_3$), 77.9 (C-2), 111.1 (C-4a), 113.4 (C-8a), 115.2 (C-7), 118.4 (C-10), 124.1 (C-9), 125.3 (C-3), 126.2 (C–Ar), 127.0 (C-4), 128.7 (2C–Ar), 129.1(2C–Ar), 137.3 (C-5a), 148.6 (C–Ar), 151.4 (C-8), 152.6 (C-10a), 159.6 (C-6). MS (*m/z*): 413 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{20}H_{14}Cl_2O_4$: C, 61.72; H, 3.63. Found: C, 61.69; H, 3.60.

*4-Chloro-8-methyl-2-(3,4-dimethoxyphenyl)-1,5-dioxa-2H-phenanthren-6-one (**3e**)* Colourless solid, yield = 80 %, mp 160–162 °C; IR (KBr) ($cm^{-1}$): 1086 (C–O–C), 1725 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, =C–$CH_3$, $J$ = 1.0 Hz), 3.87 (s, 3H, –$OCH_3$), 3.89 (s, 3H, –$OCH_3$), 5.78 (d, 1H, $H_2$, $J$ = 4.6 Hz), 6.11 (d, 1H, $H_3$, $J$ = 4.6 Hz), 6.19 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.84 (d, 1H, $H_{10}$, $J$ = 8.7 Hz), 6.86 (d, 1H, Ar–H, $J$ = 8.1 Hz), 7.00 (d, 1H, Ar–H, $J$ = 8.1), 7.26 (s, 1H, Ar–H), 7.47 (d, 1H, $H_9$, $J$ = 8.7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 19.02 ($CH_3$), 55.9 ($OCH_3$), 56.0 ($OCH_3$), 77.9 (C-2), 109.6 (C-4a), 110.4 (C-8a), 110.8 (C-7), 112.3 (C-10), 113.2 (C–Ar), 114.9 (C–Ar), 120.2 (C–Ar), 124.6 (C-9), 125.5 (C-3), 126.5 (C–Ar), 130.1 (C-4), 149.1 (C–Ar), 149.6(C–Ar), 150.2 (C-5a), 152.5 (C-8), 157.2 (C-10a), 160.0 (C-6); MS (*m/z*): 407 $(M + Na)^+$. Anal. Calcd. for $C_{21}H_{17}ClO_5$: C, 65.55; H, 4.45. Found: C, 65.50; H, 4.41.

*4,10-Dichloro-8-methyl-2-(3,4-dimethoxyphenyl)-1,5-dioxa-2H-phenanthren-6-one (**3f**)* Colourless solid, yield = 85 %, mp 158–160 °C; IR (KBr) ($cm^{-1}$): 1088 (C–O–C), 1728 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, = C-$CH_3$, $J$ = 1.0 Hz), 3.82 (s, 3H, –$OCH_3$), 3.87 (s, 3H, –$OCH_3$), 5.75 (d, 1H, $H_2$, $J$ = 4.7 Hz), 6.13 (d, 1H, $H_3$, $J$ = 4.7 Hz), 6.17 (d, 1H, $H_7$, $J$ = 1.0 Hz), 7.01(d, 1H, Ar–H, $J$ = 8.1 Hz), 7.04 (d, 1H, Ar–H, $J$ = 8.1 Hz), 7.26 (s, 1H, Ar–H), 7.48 (s, 1H, $H_9$); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.8 ($CH_3$), 53.7 ($OCH_3$), 56.3 ($OCH_3$), 76.9 (C-2), 108.9 (C-4a), 109.4 (C-8a), 110.6 (C-7), 112.8 (C-10), 113.4 (C–Ar), 115.9 (C–Ar), 121.2 (C–Ar), 123.6 (C-9), 125.7 (C-3), 126.8 (C–Ar), 130.7 (C-4), 148.1 (C–Ar), 149. 8 (C–Ar), 151.2 (C–5a), 152.7 (C-8), 156.2 (C-10a), 160.6 (C-6); MS (*m/z*): 441 $(M + Na)^+$. Anal. Calcd. for C, 60. 16; H, 3.85. $C_{21}H_{16}Cl_2O_5$. Found: C, 60.15; H, 3.81.

*4-Chloro-2-(4-fluorophenyl)-8-methyl-1,5-dioxa-2H-phenanthren-6-one (**3g**)* Colourless solid, yield = 84 %, mp 175–177 °C; IR (KBr) ($cm^{-1}$): 1085 (C–O–C), 1734 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, =C–$CH_3$, $J$ = 1.0 Hz), 5.81 (d, 1H, $H_2$, $J$ = 4.7 Hz), 6.11 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.21 (d, 1H, $H_3$, $J$ = 4.7 Hz), 6.84 (d, 1H, $H_{10}$, $J$ = 8.7 Hz), 6.92 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.35 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.45 (d, 1H, $H_9$, $J$ = 8.7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 76.2 (C-2), 109.3(C-4a), 112.3 (C-8a), 113.2 (2C-Ar), 115.6 (C-8a), 118.5 (C-10), 123.2 (C-3), 125.6 (C-9), 127.8 (2C–Ar), 129.5 (C–Ar), 136.8 (C-4), 148.4 (C-5a), 150.8 (C-8) 152.6 (C-10a), 160.2 (C-6), 161.2 (C–Ar). MS (*m/z*): 365 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{19}H_{12}ClFO_3$: C, 66.58; H, 3.53. Found: C, 66.53; H, 3.49.

*4,10-Dichloro-2-(4-fluorophenyl)-8-methyl-1,5-dioxa-2H-phenanthren-6-one (**3h**)* Colourless solid, yield = 80 %, mp 172–174 °C; IR (KBr) ($cm^{-1}$): 1088 (C–O-C), 1736 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.36 (d, 3H, = C–$CH_3$, $J$ = 1.0 Hz), 5.99 (d, 1H, $H_2$, $J$ = 5.0 Hz), 6.21 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.26 (d, 1H, $H_3$, $J$ = 5.0 Hz), 7.37 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.47 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.52 (s, 1H, $H_9$); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 76.9 (C-2), 110.0 (C-7), 111.5 (C-4a), 113.6 (C-8a), 115.1 (2C-Ar), 124.1 (C-9), 125.3(C-10), 126.2 (C-3), 128.7 (C–Ar), 129.1 (2C–Ar), 137.3 (C-4), 148.6 (C-5a), 151.4 (C-8), 152.6 (C-10a), 159.6 (C-6), 160.3 (C–Ar). MS (*m/z*): 377$(M + H)^+$ (100 %). Anal. Calcd. for $C_{19}H_{11}Cl_2FO_3$: C, 60.50; H, 2.94. Found: C, 60.46; H, 2.90.

*4-Chloro-8-methyl-2-(p-tolyl)-1,5-dioxa-2H-phenanthren-6-one (**3i**)* Colourless solid, yield = 80 %, mp 142–144 °C; IR (KBr) ($cm^{-1}$): 1086 (C–O–C), 1730 (C = O); $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H,-$CH_3$), 2.37 (d, 3H, =C–$CH_3$, $J$ = 1.0 Hz), 5.81 (d, 1H, $H_2$, $J$ = 4. 5 Hz), 6.12 (d, 1H, $H_3$, $J$ = 4.5 Hz), 6.18 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.84 (d, 1H, $H_{10}$, $J$ = 8.7 Hz), 7.17 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.33 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.45 (d, 1H, $H_9$ $J$ = 8.7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 19.0 ($CH_3$), 21.2 ($CH_3$–Ar), 77.8 (C-2), 112.3 (C-4a), 113.2 (C-8a), 115.2 (C-7), 124.6 (C-10), 125.4 (C-9), 126.2 (C-3), 126.4 (C–Ar), 127.3 (C–Ar), 129.1 (C–Ar), 129.5 (2C–Ar), 129.8 (2C–Ar), 134.9 (C-4), 139.0 (C-5a), 152.9 (C-8), 157.3 (C-10a), 160.0 (C-6). MS (*m/z*): 361 $(M + Na)^+$. Anal. Calcd. for $C_{20}H_{15}ClO_3$: C, 70.90; H, 4.46. Found: C, 70.86; H, 4.42.

*4,10-Dichloro-8-methyl-2-(p-tolyl)-1,5-dioxa-2H-phenanthren-6-one (**3j**)* Colourless solid, yield = 84 %, mp 139–141 °C; IR (KBr) ($cm^{-1}$): 1085 (C–O–C), 1734 (C=O), $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.35 (s, 3H, –$CH_3$) 2.39 (d, 3H, =C–$CH_3$, $J$ = 1.0 Hz), 6.14 (d, 1H, $H_2$, $J$ = 4.5 Hz), 6.24 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.32 (d, 1H, $H_3$, $J$ = 4.5 Hz), 7.22 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.35 (d, 2H, Ar–H, $J$ = 8.0 Hz), 7.54 (s, 1H, $H_9$); $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 75.5 (CH, C-2), 113.6 (C-4a), 115.5 (C-8a), 118.3 (C-7), 124.4 (C-10), 125.7 (C-9), 126.4 (C-3), 127.2 (C–Ar), 128.2 (C–Ar), 128.5 (C–Ar), 130.2 (C–Ar), 130.4 (C-4), 132.5 (C-5a), 134.7 (C-8), 151.3, 152.8 (C-10a), 156.5 (C-6). MS (*m/z*): 395 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{20}H_{14}Cl_2O_3$: C, 64.36; H, 3.78. Found: C, 64.33; H, 3.72.

*4-Chloro-2-(o-chlorophenyl)-8-methyl-1,5-dioxa-2H-phenanthren-6-one (**3k**)* Colourless solid, yield = 82 %, mp 156–158 °C; IR (KBr) ($cm^{-1}$): 1074 (C–O–C), 1736 (C=O); $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.41 (d, 3H, = C–$CH_3$, $J$ = 1.0 Hz), 5.87 (d, 1H, $H_2$, $J$ = 4.5 Hz), 6.15 (d, 1H, $H_3$, $J$ = 4.5 Hz), 6.21 (d, 1H, $H_7$, $J$ = 1.0 Hz), 6.89 (d, 1H, $H_{10}$, $J$ = 8.7 Hz) 7.39-7.49 (m, 5H, $H_9$, Ar–H); $^{13}$C NMR

(100 MHz, $CDCl_3$) δ: 19.0 ($CH_3$), 77.9 (C-2), 109.6 (C-4a), 112.4 (C-8a), 113.2 (C-10), 113.4 (C-7), 115.0 (C-8a), 124.6 (C-3), 125.1 (C–Ar), 125.6 (C–Ar), 126.3 (C–Ar), 126.5 (C-9), 127.0 (C–Ar), 127.2 (C-5a), 128.8 (C–Ar), 129.0 (C–Ar), 137.9 (C-4), 152.4 (C-8), 157.3 (C-10a), 160.3 (C-6). MS (*m/z*): 381 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{19}H_{12}Cl_2O_3$: C, 63.53; H, 3.37. Found: C, 63.50; H, 3.34.

*4,10-Dichloro-2-(o-chlorophenyl)-8-methyl-1,5-dioxa-2H-phenanthren-6-one (**3l**)* Colourless solid, yield = 80 %, mp 154–156 °C; IR (KBr) ($cm^{-1}$): 1080 (C–O–C), 1738 (C=O); $^1H$ NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, =C–$CH_3$, $J = 1.0$ Hz), 6.14 (d, 1H, $H_2$, $J = 4.5$ Hz), 6.23 (d, 1H, $H_7$, $J = 1.0$ Hz), 6.32 (d, 1H, $H_3$, $J = 4.5$ Hz), 7.29–7.54 (m, 4H, ArH), 7.55 (s, 1H, $H_9$); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 75.5 (C-2), 108.5 (C-4a), 113.6 (C-10), 115.3 (C-7), 118.3 (C-8a), 124.4 (C-3), 125.7 (C–Ar), 126.4 (C–Ar), 127.2 (C-9), 127.5 (C–Ar), 128.0 (C-5a), 128.2 (C–Ar), 128.5 (C–Ar), 130.2 (C-4), 132.5 (C–Ar), 151.3 (C-8), 152.8 (C-10a), 159.2 (C-6). MS (*m/z*): 415 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{19}H_{11}Cl_3O_3$: C, 57.97; H, 2.82. Found: C, 57.94; H, 2.79.

*4-Chloro-8-methyl-2-(1-naphthyl)-1,5-dioxa-2H-phenanthren-6-one (**3m**)* Colourless solid, yield = 80 %, mp 136–138 °C; IR (KBr) ($cm^{-1}$): 1084 (C–O–C), 1736 (C = O); $^1H$ NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, =C–$CH_3$, $J = 1.00$ Hz), 5.97 (d, 1H, $H_2$, $J = 4.5$ Hz), 6.21 (d, 1H, $H_7$, $J = 1.0$ Hz), 6.35 (d, 1H, $H_3$, $J = 4.5$ Hz), 7.12 (d, 1H, $H_{10}$, $J = 8.7$ Hz), 7.34–8.09 (m, 8H, $H_9$, ArH); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 19.0 ($CH_3$), 76.1 (C-2), 109.7 (C-4a), 111.6 (C-8a), 113.2 (C-7), 115.4 (C-10), 118.6 (C-3), 123.4 (C–Ar), 124.6 (C–Ar), 125.1 (C-9), 125.5 (C–Ar), 126.1 (C–Ar), 126.3 (C–Ar), 127.0 (C–Ar), 128.7 (C–Ar), 129.1 (C–Ar), 130.2 (C- Ar), 130.8 (C- Ar), 137.3 (C-4), 148.6 (C-5a), 151.4 (C-8), 152.6 (C-10a), 159.3 (C-6). MS (*m/z*): 397 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{23}H_{15}ClO_3$: C, 73.70; H, 4.03. Found: C, 73.67; H, 4.00.

*4,10-Dichloro-8-methyl-2-(1-naphthyl)-1,5-dioxa-2H-phenanthren-6-one (**3n**)* Colourless solid, yield = 80 %, mp 133–135 °C; IR (KBr) ($cm^{-1}$): 1086 (C–O–C), 1736 (C=O); $^1H$ NMR (400 MHz, $CDCl_3$) δ: 2.36 (d, 3H, =C–$CH_3$, $J = 1.0$ Hz), 6.21 (d, 1H, $H_7$, $J = 1.0$ Hz), 6.30 (d, 1H, H2, $J = 4.7$ Hz), 6.69 (d, 1H, $H_3$, $J = 4.7$ Hz), 7.40–8.38 (m, 8H, $H_9$, $H_{10}$, ArH); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 18.9 ($CH_3$), 75.9 (C-2), 111.2 (C-4a), 113.4 (C-8a), 115.2 (C-7), 118.6 (C-3), 123.8 (C-10), 124.7 (C-9), 126.0 (C–Ar), 126.1 (C–Ar), 126.1 (C–Ar), 126.8 (C–Ar), 128.8 (C–Ar), 130.2 (C–Ar), 130.8 (C–Ar), 131.6 (C–Ar), 134.1 (C-4), 148.7 (C-5a), 151.4 (C-8), 152.9 (C-10a), 159.4 (C-6). MS (*m/z*): 409 $(M + H)^+$ (100 %). Anal. Calcd. for $C_{23}H_{14}Cl_2O_3$: C, 67.50; H, 3.45. Found: C, 67.45; H, 3.41.

*4-Chloro-8-methyl-2-(thiophen-2-yl)-1,5-dioxa-2H-phenanthren-6-one (**3o**)* Colourless solid, yield = 85 %, mp 155–157 °C; IR (KBr) ($cm^{-1}$): 1082 (C–O–C), 1720 (C=O); $^1H$ NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, 3H, = C–$CH_3$, $J = 1.0$ Hz), 6.07 (d, 1H, $H_2$, $J = 4.5$ Hz), 6.19 (d, 1H, $H_7$, $J = 1.0$ Hz), 6.23 (d, 1H, $H_3$, $J = 4.5$ Hz), 6.86 (d, 1H, $H_{10}$, $J = 8.7$ Hz), 6.95–7.33 (m, 3H, Ar–H), 7.45 (d, 1H, $H_9$, $J = 8.7$ Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 19.0 ($CH_3$), 72.7 (C-2), 109.6 (C-4a), 112.4 (C-8a), 113.5 (C-7), 115.1 (C-10), 123.5 (C-3), 126.1 (C–Ar), 126.5 (C-9), 126.9 (C- Ar), 127.3 (C–Ar), 127.5 (C–Ar), 140.4 (C-4), 150.2 (C-5a), 152.4 (C-8), 156.6 (C-10a), 159.9 (C-6). MS (*m/z*): 353 $(M + Na)^+$ (100 %). Anal. Calcd. for $C_{17}H_{11}ClO_3S$: C, 61.73; H, 3.35. Found: C, 61.69; H, 3.31.

## Conclusion

We synthesized a new series of compounds **3a–o** under conventional and microwave irradiation methods. In microwave irradiation method, reactions were completed in short time with better yields compared to conventional method. All the new compounds have been screened for antimicrobial activity. The compounds **3e**, **3f**, **3o** were more potent and the compounds **3f**, **3j** were moderately potent for pathogenic bacteria where as the compounds **3e**, **3o** were more potent and the compounds **3f**, **3j** were moderately potent for pathogenic fungi compared to the standard drugs with their respective concentrations.

**Acknowledgments** The authors are thankful to The Head, Department of Chemistry, Osmania University, Hyderabad for providing Laboratory facilities and one of the authors B. Vijaya Lakshmi, thankful to CSIR, New Delhi, India for financial support in the form of CSIR-SRF. We also thankful to The Director, CFRD, Osmania University, Hyderabad for providing elemental and spectral analysis facilities.

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