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# Synthesis of Functionalized Benzo[*f*]2*H*-Chromenes and Evaluation of Their Antimicrobial Activities[1]

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**Abstract**—Knoevenagel cyclocondensations of α-hydroxy naphthaldehyde with β-oxodithioesters and ketene dithioacetals yielded 2*H*-benzo[*f*]chromene-2-thiones and 2*H*-benzo[*f*]chromen-2-ones, respectively, in high yields. The newly synthesized compounds were evaluated for antifungal and antibacterial activities. Among them, compounds (2-furyl)(3-thioxo-3*H*-benzo[*f*]chromen-2-yl)methanone and phenyl(3-oxo-3*H*-benzo[*f*]chromen-2-yl)methanone exhibited excellent antifungal activity against tested fungi *Curvularia lunata* and *Fusarium moniliforme*. The highest antibacterial activity against the tested bacteria *Escherichia coli* and *Staphylococcus aureus* was observed for (4-chlorophenyl)(3-oxo-3*H*-benzo[*f*]chromen-2-yl)methanone. The results of antimicrobial screening demonstrate that (2-furyl)(3-thioxo-3*H*-benzo[*f*]chromen-2-yl)methanone, phenyl(3-oxo-3*H*-benzo[*f*]chromen-2-yl)methanone, and (4-chlorophenyl)(3-oxo-3*H*-benzo[*f*]chromen-2-yl)methanone are promising as antimicrobial drugs.

*Keywords:* chromene, piperidine, antimicrobial activity, β-oxodithioesters, cyclocondensation

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## INTRODUCTION

Chromenes constitute a major class of naturally occurring heterocyclic compounds that display a wide range of biological and therapeutic properties [1–5]. They are also used as additives in food, perfumes, cosmetics, optical brighteners, and dispersed fluorescent and laser dyes, antitumor and anti-HIV therapy, and as CNS stimulants [6–8].

Though classical condensation processes like Pechmann, Perkin, Reformatsky, Wittig, and Knoevenagel reactions are available for the synthesis of coumarinyl derivatives [1, 9], many improved methodologies have been introduced to make the classical routes more efficacious [10–13]. A limitation of these classical routes is the confinement to certain starting materials, such as methyl- and ethylacetoacetate, malononitrile, and Meldrums acid. Surprisingly, newly established synthons, like β-oxodithioesters and α-oxoketenedithioacetals, have not been introduced yet in the family of these starting materials. Recently, we have reported the radical scavenging potential of some 3-heteroaroyl-2*H*-chromene-2-thiones synthesized from β-oxodithioesters and salicylaldehyde toward the stable free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) [14].

In continuation of our interest in the synthesis of bioactive heterocycles using these new synthons [14–17], here we report a facile synthesis of 2*H*-benzo[*f*]chromene-2-thiones and 2*H*-benzo[*f*]chromen-2-ones from β-oxodithioesters and α-oxoketenedithioacetals, respectively, by the domino Knoevenagel cyclocondensations (Scheme 1). A critical report on their antimicrobial activities against the *Staphylococcus aureus* (MTCC-7443) and *Escherichia coli* (MTCC-725) and two fungal species, namely *Curvularia lunata* (MTCC-2605) and *Fusarium moniliforme* (MTCC-278), is also presented.

[1] The article is published in the original.

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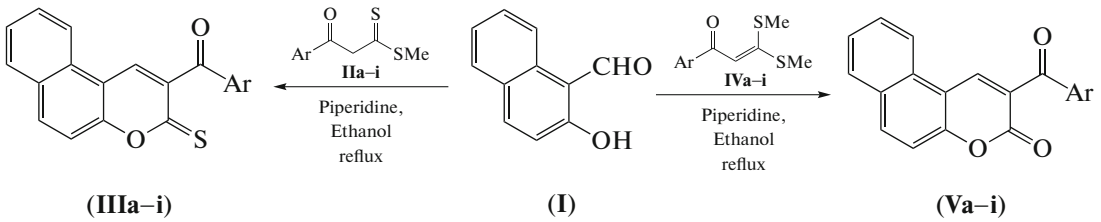
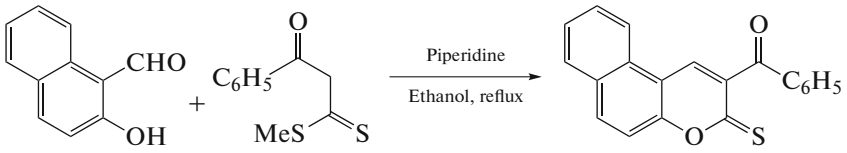



**Scheme 1.** Synthesis of 2*H*-benzo[*f*]chromene-2-thiones and 2*H*-benzo[*f*]chromen-2-ones from β-oxodithioesters and α-oxoketenedithioacetals.

## RESULTS AND DISCUSSION

### *Chemistry*

In our initial investigation, we have chosen 2-hydroxy-1-naphthaldehyde (**Ia**) and β-oxodithioester (**IIa**) (methyl-3-oxo-3-phenylpropanedithioate) as model substrates for the cyclocondensation reaction. By simply refluxing their molar equivalent mixture in ethanol at 95°C with piperidine as a catalyst, the desired product 3-(benzoyl)-2*H*-benzo[*f*]chromene-2-thione (**IIIa**) was obtained in 93% yield (Scheme 2).




(I) (IIa) (IIIa)

**Scheme 2.** Synthesis of 3-(benzoyl)-2*H*-benzo[*f*]chromene-2-thione (**IIIa**).

The condensation of starting compound (**I**) with compound (**II**) to generate chromene (**IIIa**) was investigated under a variety of conditions and the results are presented in Table 1. In ethanol, the condensation took place even with a catalytic amount of piperidine (0.2 mmol; entry 1, Table 1), whereas no product was obtained in aqueous medium. A control experiment in the absence of the catalyst provided no product. Other bases, like triethylamine, were also tested in ethanol with negligible yield of product, even though they afforded 40% yield in combination of other solvents, e.g. DMF and THF. We further carried out the same condensation reaction using various metal salt catalytic systems. Among them, cupric chloride and aluminum chloride gave good yields, however, the reaction took longer time (4 h) and the yields were poorer in comparison with piperidine.

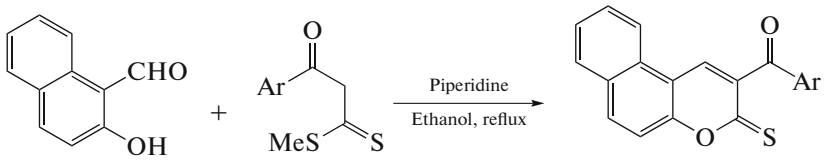
After optimization of the reaction conditions, the generality and scope of the condensation reaction were evaluated. The process was successfully extended to a wide range of β-oxodithioesters (**IIb–i**) and 2-hydroxy-1-naphthaldehyde to afford the corresponding chromenes (**IIIb–i**) in excellent yields (Table 2).

In order to evaluate the further scope of the reaction, we used α-oxoketene dithioacetals instead of β-oxodithioester. Interestingly, the cyclocondensation reacitons of 2-hydroxy-1-naphthaldehyde (**I**) with α-oxoketenedithioacetals (**IVa–i**) were also found successful affording 2*H*-benzo[*f*]chromen-2-ones (**Va–i**) (Table 2).

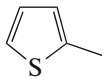
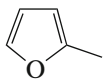
**Table 1.** Evaluation of different catalytic systems in optimization of the chromene synthesis

| Entry | Catalyst (equiv.) | Solvent | Yield, % |
|---|---|---|---|
| 1 | Piperidine (0.2 mmol) | EtOH | 93 |
| 2 | Piperidine (0.1 mmol) | EtOH | 90 |
| 3 | Piperidine | Water | No reaction |
| 4 | No catalyst | – | No reaction |
| 5 | $Et_3N$ (0.2 mmol) | THF/DMF | 40 |
| 6 | $CuCl_2$ | – | 70 |
| 7 | $AlCl_3$ | – | 68 |

**Table 2.** Piperidine-catalyzed synthesis of coumarins (**IIIa–i**) in ethanol[a]

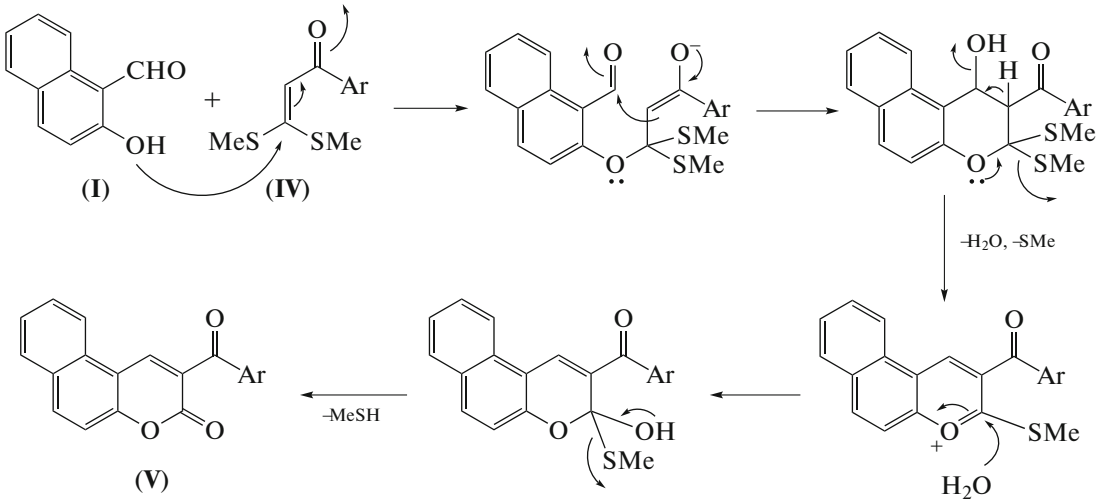



**(I)** **(IIa–i)** **(IIIa–i)**

| Entry | Ar | Products | Yields |
|---|---|---|---|
| 1 | $C_6H_5$ | **(IIIa)** | 93 |
| 2 | 4-$MeOC_6H_4$ | **(IIIb)** | 95 |
| 3 | 4-$MeC_6H_4$ | **(IIIc)** | 94 |
| 4 | 4-$ClC_6H_4$ | **(IIId)** | 90 |
| 5 | 4-$BrC_6H_4$ | **(IIIe)** | 93 |
| 6 |  | **(IIIf)** | 85 |
| 7 |  | **(IIIg)** | 80 |
| 8 | 4-$FC_6H_4$ | **IIIh** | 86 |
| 9 | 2,4-$Cl_2C_6H_3$ | **IIIi** | 92 |

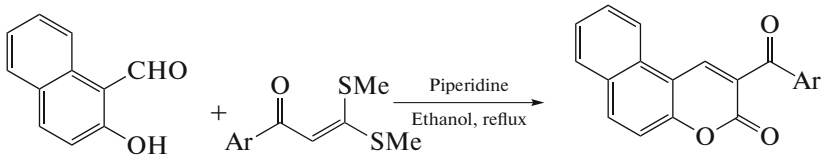
[a]Reaction conditions: (**I**) (2.5 mmol), (**II**) (2.5 mmol), piperidine (0.2 mmol), 95°C, 10–15 min.

Thus, in the presence of catalytic amount of piperidine, α-oxoketenedithioacetal (**IVa**) was heated with 2-hydroxy-1-naphthaldehyde (**Ia**) at 95°C with ethanol. The progress of the reaction was monitored by TLC and complete transformation was observed in 1 h. The reaction mixture was then poured into crushed ice and the solid product was separated, filtered, and recrystallized from ethanol. The reaction went very smoothly and the yellow crystal of coumarin (**Va**) were obtained in 80% yield (Table 3, entry 1), the structure of which was confirmed by spectral and analytical data. The reaction was also extended to different α-oxoketenedithioacetals (**IVb–i**) to afford coumarins (**Vb–i**) in good-to-excellent yield. The thiomethyl groups were replaced by the naphthyl hydroxyl and during the cyclization the subsequent dethiomethylation process led to the sulfur-free chromene compound (**V**) as shown in the plausible mechanism (Scheme 3).

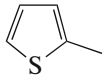
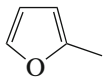



**Scheme 3.** Plausible mechanism for the formation of benzo[*f*]chromene (**V**).

**Table 3.** Piperidine catalyzed synthesis of chromenes (**Va–f**)[a]




**(I)** **(IVa–i)** **(IIIa–i)**

| Entry | Arya | Products | Yields |
|---|---|---|---|
| 1 | 4-$FC_6H_5$ | **(Va)** | 80 |
| 2 | 4-$MeC_6H_4$ | **(Vb)** | 87 |
| 3 | 4-$BrC_6H_4$ | **(Vc)** | 82 |
| 4 | 4-$ClC_6H_4$ | **(Vd)** | 83 |
| 5 | $C_6H_5$ | **(Ve)** | 88 |
| 6 | 4-$MeOC_6H_4$ | **(Vf)** | 86 |
| 7 |  | **(Vg)** | 79 |
| 8 |  | **(Vh)** | 75 |
| 9 | 2,4-$Cl_2C_6H_3$ | **(Vi)** | 82 |

[a]Reaction conditions: (**I**) (2.5 mmol), (**IV**) (2.5 mmol), piperidine (2 mmol), 90°C, 1–2 h.

*Pharmacology*

**Antifungal activities** of 18 compounds were tested against two fungal strains *Curvularia lunata* and *Fusarium moniliforme*. There were variations in mycelia growth inhibition (%) with varying concentration of the compounds. Compounds (**IIIe**) (3-(4-bromobenzoyl)-2*H*-benzo[*f*]chromene-2-thione), (**IIIf**) (3-thienyl-2*H*-benzo[*f*]chromene-2-thione), (**IIIg**) (3-(2-furyl)-2*H*-benzo[*f*]chromene-2-thione), (**Vb**) (3-(4-methylbenzoyl-2*H*-benzo[*f*]chromen-2-one), and (**Vd**) (3-(4-chlorobenzoyl-2*H*-benzo[*f*]chromen-2-one) were effective against fungus *C. lunata* (the results are shown in Fig. 1). Significant mycelial growth inhibition of 90% and above was found for compounds (**IIIe**), (**IIIf**), (**IIIg**), and (**Ve**) at 500 μg/mL concentration. Compound (**IIIg**) had very efficient antifungal activity (98% mycelia inhibition even at 200 μg/mL).

Among the compounds tested for antifungal activity against *F. moniliforme,* compounds (**IIIa**), (**IIIe**), (**IIIf**), and (**Ve**) showed significant activity as depicted in Fig. 2. There was increase in the inhibition of mycelia growth at higher concentration (500 μg/mL) as compared to lower concentrations (100 and 200 μg/mL). Mycelial inhibition of 90% and above was found for compounds (**IIIe**), (**IIIf**), and (**Ve**). Also, 100% mycelium inhibition of *F. moniliforme* was shown by compound (**Ve**).

Compounds (**IIIg**) and (**Ve**) showed excellent antifungal activity, the % inhibition of the tested fungi being more or similar to that of the antifungal activity of standard antifungal agent fluconazole.

**Antibacterial activity.** Among the 18 compounds tested, only 4 compounds (**IIIc**), (**IIIe**), (**IIIf**), and (**Vd**) showed efficient antibacterial activity against the bacteria *Escherichia coli* and *Staphylococcus aureus* at 500 μg/mL concentration (Fig. 3). Negligible antibacterial activity was observed at lower concentrations (100 and 200 μg/mL). Compound (**Vd**) showed highest antibacterial activity (zone of inhibition of 15 mm for *E. coli* and 19 mm for *S. aureus* were quite reasonable as compared to the standard drug streptomycin).

## EXPERIMENTAL

*Chemistry*

The melting points were determined on a Meltemp II laboratory device and are uncorrected. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker FT-NMR-DRX300 (300 and 75.5 MHz, respectively) in $CDCl_3$ and chemical shifts are reported in parts per million (δ, ppm) and signals are quoted as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and dd (doublet of doublets). The FT-IR spectra ($\nu_{max}$, $cm^{-1}$) were recorded on a Perkin-Elmer FT-IR spectrometer (KBr). Elemental analyses were recorded using a Perkin-Elmer 2400 analytical instrument. Mass spectra (ESI-MS) were recorded on a Waters Q-TOF LC-MS

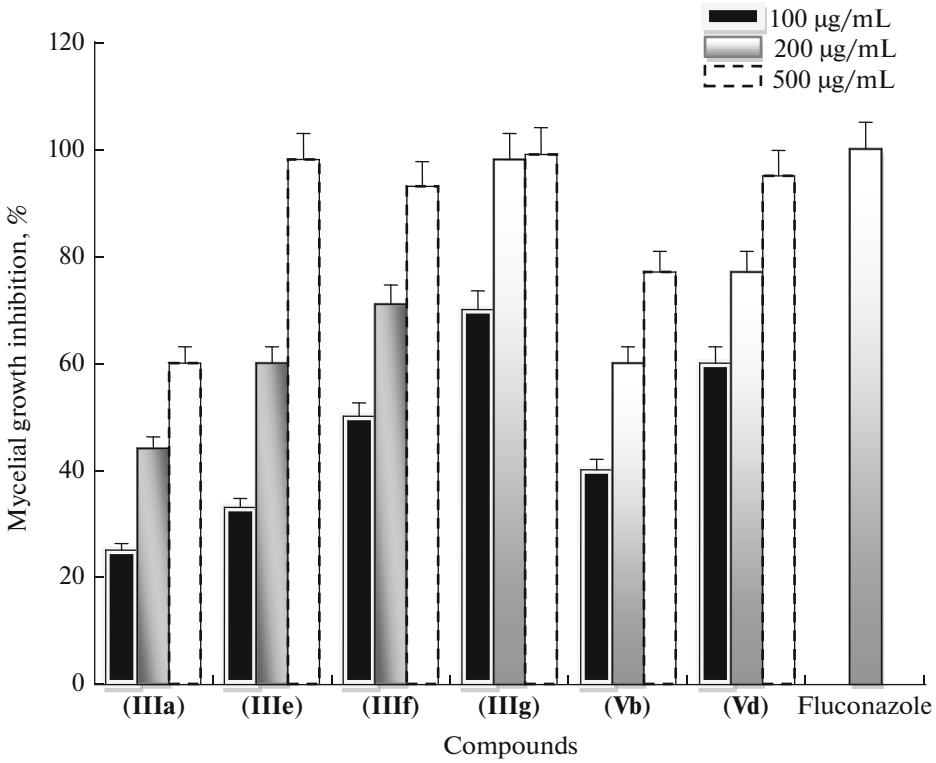



**Fig. 1.** Inhibition of *C. lunata* mycelium growth (%) by the synthesized compounds.

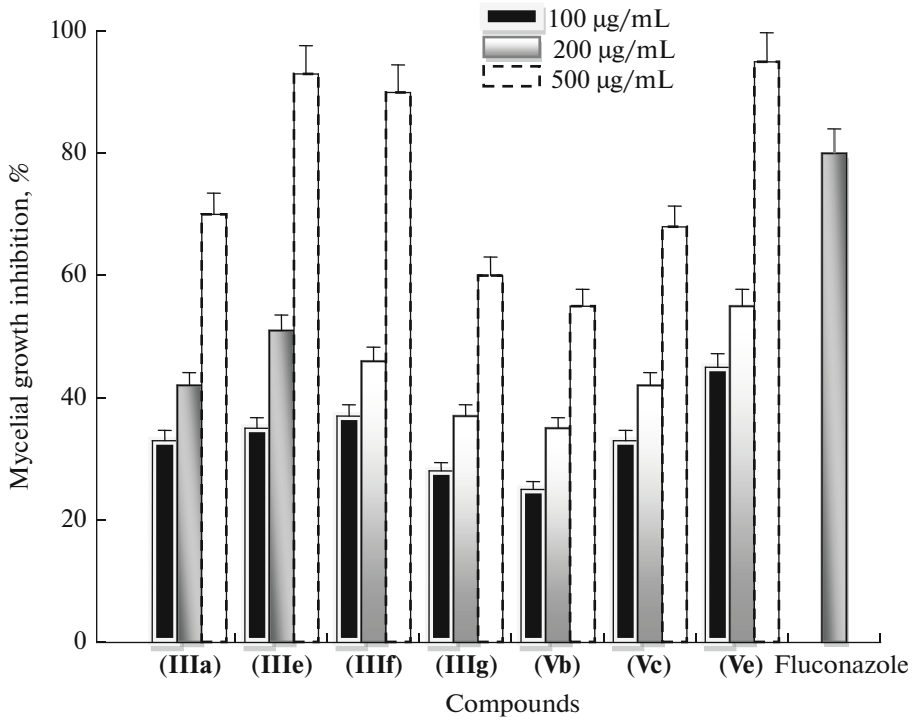



**Fig. 2.** Inhibition of *F. moniliforme* mycelium growth (%) by the synthesized compounds.

spectrometer. Analytical thin layer chromatography (TLC) was carried out using pre-coated silica gel glass plates (E. Merck, Kiesegel 60F254). β-Oxodithioesters were prepared by known procedures [14–16].

### *General Procedure for the Synthesis of Chromenes (**IIIa–i**)*

To a stirred solution of 2-hydroxynapthaldehyde (**I**) (2.2 mmol) and β-oxodithioesters (**IIa–i**) (2.2 mmol)

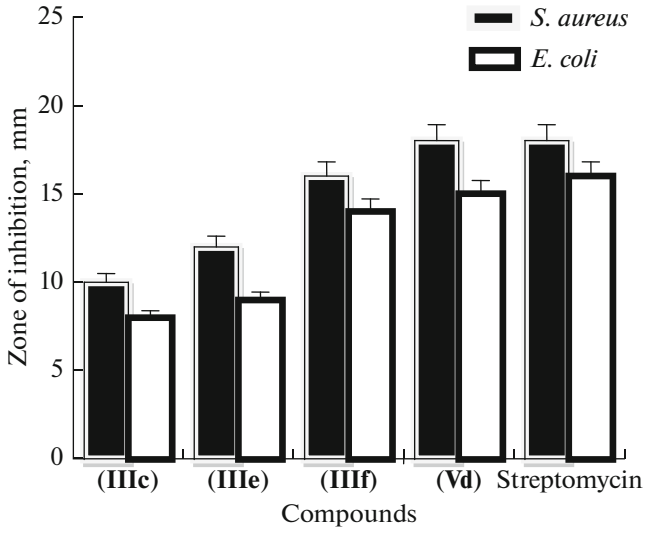



**Fig. 3.** Antibacterial activity of the synthesized compounds.

in EtOH, piperidine (0.22 mmol) was added at room temperature. The reaction mixture was heated at refluxing temperature in a preheated oil bath (95°C) for 10–15 min for completion of the reaction (TLC; hexane–EtOAc, 8 : 2). The reaction mixture was then diluted with ethylacetate (25 mL) and the organic solution was washed sequentially with water (3 × 25 mL) and brine (2 × 10 mL) and dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure in a rotavapor and the resulted crude was subjected to column chromatography on $SiO_2$. Separation was done using increasing amounts of ethyl acetate in hexane as eluent.

**3-(Benzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIIa).** Yellow crystals, mp 200–201°C. $^1$H NMR: 7.50–7.56 (m, 3H, ArH), 7.61–7.69 (m, 2H, ArH), 7.73–7.78 (m, 1H, ArH), 7.94–8.02 (m, 3H, ArH), 8.13 (d, $J$ = 9 Hz, 1H, ArH), 8.26–8.30 (m, 1H, ArH), 8.40 (s, 1H, ArH); $^{13}$C NMR: 112.7, 116.5, 121.5, 125.4, 126.5, 128.7, 128.9, 129.4, 129.7, 129.9, 130.7, 134.8, 135.4, 138.9, 141.8, 157.8, 192.1, 192.7; IR: 1265, 1560, 1654, 3056; MS, *m/z*: 316 ($M^+$). Anal. calcd. for $C_{20}H_{12}O_2S$: C, 75.93; H, 3.82; S, 10.14. Found: C, 75.95; H, 3.85; S, 10.11.

**3-(4-Methoxybenzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIIb).** Yellow crystals, mp 218–219°C. $^1$H NMR: 3.80 (s, 3H, $OCH_3$), 6.87 (d, $J$ = 6.6 Hz, 2H, ArH), 7.54–7.65 (m, 3H, ArH), 7.87–7.89 (m, 3H, ArH), 8.03 (d, $J$ = 6.9 Hz, 1H, ArH), 8.15 (d, $J$ = 6.6 Hz, 1H, ArH), 8.27 (s, 1H, ArH); $^{13}$C NMR: 113.91, 114.12, 115.26, 121.53, 127.06, 128.81, 128.91, 128.95, 129.22, 129.25, 129.35, 129.65, 130.68, 134.65, 139.16, 157.64, 164.34, 191.29, 192.73; MS, *m/z*: 346 ($M^+$). Anal. calcd. for $C_{21}H_{14}O_3S$: C, 72.81; H, 4.07; S, 9.26. Found: C, 72.79; H, 4.05; S, 9.29.

**3-(4-Methylbenzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIIc).** Yellow solid, mp 264–265°C. $^1$H NMR: 2.43 (s, 3H, $CH_3$), 7.27 (d, $J$ = 10.8 Hz, 2H, ArH), 7.75–7.61 (m, 3H, ArH), 7.89 (d, $J$ = 8.1 Hz, 2H, ArH), 7.96 (d, $J$ = 8.1 Hz, 1H, ArH), 8.11 (d, $J$ = 9.3 Hz, 1H, ArH), 8.24 (d, $J$ = 8.1 Hz, 1H, ArH), 8.36 (s, 1H, ArH). $^{13}$C NMR: 192.6, 192.3, 157.0, 145.1, 139.1, 134.6, 133.2, 130.6, 129.9, 129.7, 129.5, 129.2, 128.9, 128.8, 127.0, 121.6, 116.5, 115.2, 21.8. MS, *m/z*: 330 ($M^+$). Anal. calcd. for $C_{21}H_{14}O_2S$: C, 76.34; H, 4.20. Found C, 76.33; H, 4.19.

**3-(4-Chlorobenzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIId).** Yellow crystals, mp 272–273°C. $^1$H NMR: 7.47 (d, $J$ = 8.4 Hz, 2H, ArH), 7.66–7.69 (m, 2H, ArH), 7.74–7.79 (m, 1H, ArH), 7.92–8.01 (m, 3H, ArH), 8.15 (d, $J$ = 9 Hz, 1H, ArH), 8.27 (d, $J$ = 8.1 Hz, 1H, ArH), 8.42 (s, 1H, ArH); $^{13}$C NMR: 115.2, 116.5, 121.7, 127.1, 128.9, 129.1, 129.2, 129.3, 130.4, 130.7, 131.0, 134.3, 135.0, 138.5, 140.4, 157.9, 191.6, 192.4; IR: 1259, 1558, 1666, 3083; MS, *m/z*: 350 ($M^+$). Anal. calcd. for $C_{20}H_{11}ClO_2S$: C, 68.47; H, 3.16; S, 9.14. Found: C, 68.49; H, 3.11; S, 9.19.

**3-(4-Bromobenzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIIe).** Yellow crystals, mp 269–270°C. $^1$H NMR: 7.64 (d, $J$ = 8.3 Hz, 2H, ArH), 7.67–7.7 (m, 2H, ArH), 7.72–7.76 (m, 1H, ArH), 7.91–8.08 (m, 3H, ArH), 8.14 (d, $J$ = 9 Hz, 1H, ArH), 8.28 (d, $J$ = 8.1 Hz, 1H, ArH), 8.10 (s, 1H, ArH); $^{13}$C NMR: 114.6, 116.1, 121.4, 127.3, 128.4, 129.7, 129.9, 130.3, 130.5, 130.7, 131.5, 133.9, 134.6, 137.9, 140.1, 157.4, 191.1, 193.2; IR: 1270, 1601, 1672, 3071; MS, *m/z*: 350 ($M^+$). Anal. calcd. for $C_{20}H_{11}BrO_2S$: C, 60.77; H, 2.81. Found: C, 60.75; H, 2.80.

**3-(2-Thienyl)-2*H*-benzo[*f*]chromene-2-thione (IIIf).** Yellow crystals, mp 250–251°C. $^1$H NMR: 7.17–7.28 (m, 2H, ArH), 7.65–7.80 (m, 4H, ArH), 7.97 (d, $J$ = 7.8 Hz, 1H, ArH), 8.13 (d, $J$ = 9 Hz, 1H, ArH), 8.25 (d, $J$ = 8.1 Hz, 1H), 8.40 (s, 1H, ArH); $^{13}$C NMR: 115.0, 116.5,121.7, 127.1, 128.5, 128.9, 129.3, 129.4, 130.7, 134.9, 135,1, 135.6, 138.6, 142.9, 157.7, 174.4, 184.7, 192.3; IR: 1271, 1558, 1637, 3055; MS, *m/z*: 322 ($M^+$). Anal. calcd. for $C_{18}H_{10}O_2S_2$: C, 67.06; H, 3.13; S, 19.89. Found: C, 67.09; H, 3.15; S, 19.83.

**3-(2-Furyl)-2*H*-benzo[*f*]chromene-2-thione (IIIg).** Yellow crystals, mp 252–253°C. $^1$H NMR: 6.61–6.59 (m, 1H, ArH) 7.33 (d, $J$ = 3.6 Hz, 1H, ArH), 7.76–7.62 (m, 4H, ArH), 7.96 (d, $J$ = 7.8 Hz, 1H, ArH), 8.11 (d, $J$ = 9.0 Hz, 1H, ArH), 8.25 (d, $J$ = 8.1 Hz, 1H, ArH), 8.39 (s, 1H, ArH); $^{13}$C NMR: 112.8, 115.0, 116.4, 120.1, 121.6, 127.0, 127.0, 128.8, 129.0, 129.2, 130.0, 130.6, 134.9, 137.7, 147.5, 151.8, 157.7, 179.9, 192.3; IR: 1641, 1558, 1462, 1284, 1170; MS, *m/z*: 307 ($M^+$). Anal. calcd. for $C_{18}H_{10}O_3S$: C, 70.57; H, 3.29. Found: C, 70.59; H, 3.31.

**3-(4-Fluorobenzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIIh).** Yellow crystals, mp 269–270°C. $^1$H NMR: 6.47

(d, $J$ = 8.4 Hz, 2H, ArH), 7.65–7.69 (m, 2H, ArH), 7.67–7.68 (m, 1H, ArH), 7.91–8.10 (m, 3H, ArH), 8.13 (d, $J$ = 9 Hz, 1H, ArH), 8.18 (d, $J$ = 8.1 Hz, 1H, ArH), 8.23 (s, 1H, ArH); $^{13}$C NMR: 116.2, 116.5, 122.5, 126.5, 127.9, 128.8, 129.6, 129.8, 130.5, 130.9, 132.0, 135.1, 134.9, 138.7, 140.8, 156.8, 190.4, 193.5; IR: 1263, 1543, 1665, 3070; MS, *m/z*: 334.4 ($M^+$). Anal. calcd. for $C_{20}H_{11}FO_2S$: C, 71.84; H, 3.32. Found: C, 71.82; H, 3.30.

**3-(2,4-Dichlorobenzoyl)-2*H*-benzo[*f*]chromene-2-thione (IIIi).** Yellow crystals, mp 275–276°C. $^1$H NMR: 7.47 (d, $J$ = 8.4 Hz, 2H, ArH), 7.66–7.69 (m, 2H, ArH), 7.74–7.78 (m, 1H, ArH), 7.87–7.96 (m, 2H, ArH), 8.22 (d, $J$ = 9 Hz, 1H, ArH), 8.28 (d, $J$ = 8.1 Hz, 1H, ArH), 8.83 (s, 1H, ArH); $^{13}$C NMR: 114.2, 115.8, 120.8, 125.1, 126.9, 128.6, 129.4, 129.7, 130.8, 131.4, 131.9, 133.3, 134.6, 137.5, 139.4, 149.7, 190.1, 192.8; IR: 1280, 1579, 1664, 3028; MS, *m/z*: 350 ($M^+$). Anal. calcd. for $C_{20}H_{10}Cl_2O_2S$: C, 68.47; H, 3.16; S, 9.14. Found: C, 68.49; H, 3.11; S, 9.19.

*General Procedure for Synthesis of Chromenes (**Va–i**)*

To a stirred solution of 2-hydroxynapthaldehyde (**I**) (2.2 mmol) and α-oxoketenedithioacetal (**IIa–i**) (2.2 mmol) in EtOH (30 mL), piperidine (0.22 mmol) was added at room temperature. The reaction mixture was heated at reflux in a preheated oil bath (95°C) for 1–1.5 h for completion of the reaction (TLC; hexane–EtOAc, 8 : 2). The reaction mixture was then diluted with ethylacetate (25 mL), and the organic solution was washed sequentially with water (3 × 25 mL) and brine (2 × 10 mL) and dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure in a rotavapor and the resulted crude was subjected to column chromatography on $SiO_2$. Separation was done using increasing amounts of ethyl acetate inhexane as eluent.

**3-(4-Flurobenzoyl)-2*H*-benzo[*f*]chromen-2-one (Va).** Yellow crystals, mp 229–230°C. $^1$H NMR: 7.67 (d, $J$ = 8.2 Hz, 2H, ArH), 7.76 (d, $J$ = 9.1 Hz, 1H, ArH), 7.89 (t, $J$ = 7.8 Hz, 1H, ArH), 7.63 (t, $J$ = 7.4 Hz, 1H, ArH), 7.92 (d, $J$ = 8.9 Hz, 2H, ArH), 7.99 (d, $J$ = 8.1 Hz, 1H, ArH), 8.26 (d, $J$ = 8.9 Hz, 1H, ArH), 8.76 (d, $J$ = 8.8 Hz, 1H, ArH), 8.93 (s, 1H, ArH); $^{13}$C NMR: 111.4, 114.2, 123.4, 125.1, 126.7, 128.3, 129.4, 129.6, 129.9, 130.6, 130.9, 134.3, 135.5, 140.7, 141.5, 155.9, 158.1, 190.0, IR: 3050, 2986, 1718, 1655; MS, *m/z*: 318 ($M^+$). Anal. calcd. for $C_{20}H_{11}FO_3$: C, 75.46; H, 3.48. Found: C, 75.44; H, 3.47.

**3-(4-Methylbenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vb).** Yellow crystals, mp 191–192°C. $^1$H NMR: 2.45 (s, 3H, $CH_3$), 7.29 (d, $J$ = 8.3 Hz, 2H, ArH), 7.51 (d, $J$ = 9.3 Hz, 1H, ArH), 7.61 (br t, $J$ = 7.8 Hz, 1H, ArH), 7.71 (br t, $J$ = 7.3 Hz, 1H, ArH), 7.83 (d, $J$ = 8.3 Hz, 2H, ArH), 7.94 (d, $J$ = 8.3 Hz, 1H, ArH), 8.11 (d, $J$ = 9.3 Hz, 1H, ArH), 8.25 (d, $J$ = 8.8 Hz, 1H, ArH), 8.90 (s, 1H, ArH); $^{13}$C NMR: 21.8, 112.7, 116.7, 121.5, 125.6, 126.5, 128.9, 129.2, 129.3, 129.4, 129.8, 130.3, 133.8, 135.2, 141.4, 144.8, 155,3, 158.6, 191.7; IR: 3063, 2953, 1703, 1651; MS, *m/z*: 314 ($M^+$). Anal. calcd. for $C_{21}H_{14}O_3$: C, 80.24; H, 4.49; O, 15.27. Found: C, 80.25; H, 4.48; O, 15.29.

**3-(4-Bromobenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vc).** Yellow crystals, mp 243–244°C. $^1$H NMR: 6.43 (d, $J$ = 8.7 Hz, 2H, ArH), 7.62 (d, $J$ = 9.1 Hz, 1H, ArH), 7.64 (t, $J$ = 7.8 Hz, 1H, ArH), 7.69 (t, $J$ = 7.3 Hz, 1H, ArH), 7.76 (d, $J$ = 8.4 Hz, 2H, ArH), 7.85 (d, $J$ = 8.2 Hz, 1H, ArH), 7.93 (d, $J$ = 8.3 Hz, 1H, ArH), 8.12 (d, $J$ = 8.4 Hz, 1H, ArH), 8.34 (s, 1H, ArH); $^{13}$C NMR: 112.3, 116.5, 121.7, 124.7, 126.5, 127.7, 129.4, 129.6, 129.8, 130.6, 130.8, 132.3, 134.6, 141.1, 142.7, 148.6, 154.6, 190.0; IR: 3034, 2921, 1712, 1665; MS, *m/z*: 379 ($M^+$). Anal. calcd. for $C_{20}H_{11}BrO_3$: C, 63.35; H, 2.92; Found: C, 63.34; H, 3.33.

**3-(4-Chlorobenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vd).** Yellow crystals, mp 231–232°C. $^1$H NMR: 7.47 (d, $J$ = 8.8 Hz, 2H, ArH), 7.52 (d, $J$ = 9.3 Hz, 1H, ArH), 7.63 (t, $J$ = 7.9 Hz, 1H, ArH), 7.75 (t, $J$ = 7.3 Hz, 1H, ArH), 7.86 (d, $J$ = 8.8 Hz, 2H, ArH), 7.96 (d, $J$ = 8.3 Hz, 1H, ArH), 8.13 (d, $J$ = 8.8 Hz, 1H, ArH), 8.28 (d, $J$ = 8.3 Hz, 1H, ArH), 8.97 (s, 1H, ArH); $^{13}$C NMR: 112.7, 116.7, 121.5, 124.7, 126.7, 128.9, 129.1, 129.3, 129.4, 130.3, 130.9, 134.8, 135.8, 140.2, 142.6, 155.6, 158.6, 191.0; IR: 3069, 2951, 1707, 1655; MS, *m/z*: 334 ($M^+$). Anal. calcd. for $C_{20}H_{11}ClO_3$: C, 71.76; H, 3.31; O, 14.34. Found: C, 71.77; H, 3.33; O, 14.33.

**3-(Benzoyl)-2*H*-benzo[*f*]chromen-2-one (Ve).** Yellow crystals. mp 215–216°C. $^1$H NMR: 7.45–7.51 (m, 3H, ArH), 7.57–7.65 (m, 2H, ArH), 7.7 (t, $J$ = 7.3 Hz, 1H, ArH), 7.89–7.94 (m, 3H, ArH), 8.08 (d, $J$ = 9.3 Hz, 1H, ArH), 8.24 (d, $J$ = 8.4 Hz, 1H, ArH), 8.89 (s, 1H, ArH); $^{13}$C NMR: 112.6, 116.7, 121.5, 125.4, 126.5, 128.5, 128.9, 129.2, 129.4, 129.6, 130.3, 133.6, 135.3, 136.5, 141.7, 155.4, 158.5, 192.1; IR: 3102, 2959, 1700, 1654; MS, *m/z*: 300 ($M^+$). Anal. calcd. for $C_{20}H_{12}O_3$: C, 79.99; H, 4.03; O, 15.98. Found: C, 79.95; H, 4.02; O, 15.99.

**3-(4-Methoxybenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vf).** Yellow crystals, mp 231–232°C. $^1$H NMR: 3.82 (s, 3H, $OCH_3$), 6.89 (d, $J$ = 8.3 Hz, 2H, ArH), 7.51 (d, $J$ = 9.3 Hz, 1H, ArH), 7.57 (br t, $J$ = 7.8 Hz, 1H, ArH), 7.67 (br t, $J$ = 7.3 Hz, 1H, ArH), 7.85 (d, $J$ = 8.3 Hz, 2H, ArH), 7.91 (d, $J$ = 8.3 Hz, 1H, ArH), 8.07 (d, $J$ = 9.3 Hz, 1H, ArH), 8.19 (d, $J$ = 8.8 Hz, 1H, ArH), 8.79 (s, 1H, ArH); $^{13}$C NMR: 55.6, 112.7, 113.9, 116.7, 121.5, 125.9, 126.5, 128.9, 129.1, 129.2, 129.3, 130.3, 132.2, 135.1, 141.2, 155.2, 158.8, 164.2, 190.5; IR: 3065, 2950, 1706, 1656; MS, *m/z*: 330 ($M^+$). Anal. calcd. for $C_{21}H_{14}O_4$: C, 76.35; H, 4.27; O, 19.37. Found: C, 76.37; H, 4.26; O, 19.39.

**3-(2-Thienylbenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vg).** Yellow crystals, mp 240–241°C. $^1$H NMR: 7.17–

7.28 (m, 2H, ArH), 7.65–7.80 (m, 4H, ArH), 7.97 (d, $J$ = 7.8 Hz, 1H, ArH), 8.13 (d, $J$ = 9 Hz, 1H, ArH), 8.25 (d, $J$ = 8.1 Hz, 1H, ArH), 8.40 (s, 1H, ArH); $^{13}$C NMR: 115.0, 116.5,121.7, 127.1, 128.5, 128.9, 129.3, 129.4, 130.7, 134.9, 135,1, 135.6, 138.6, 142.9, 150.5, 157.7, 174.4, 192.3; IR: 1271, 1558, 1637, 3055; MS, $m/z$: 322 ($M^+$). Anal. calcd. for $C_{18}H_{10}O_3S$: C, 70.57; H, 3.29. Found: C, 69.09; H, 3.25.

**3-(2-Furylbenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vh).** Yellow crystals, mp 240–241°C. $^1$H NMR: 6.61–6.59 (m,1H, ArH), 7.33 (d, $J$ = 3.6 Hz, 1H, ArH), 7.76–7.62 (m, 4H, ArH), 7.96 (d, $J$ = 7.8 Hz, 1H, ArH), 8.11 (d, $J$ = 9.0 Hz, 1H, ArH), 8.39 (s, 1H, ArH), 8.25 (d, $J$ = 8.1 Hz, 1H, ArH); $^{13}$C NMR: 112.8, 115.0, 116.4, 120.8, 121.9, 127.7, 129.0, 129.6, 129.9, 130.6, 131.0, 135.2, 137.8, 147.6, 156.5, 157.7, 170.8, 189.9; IR: 1291, 1555, 1632, 3050; MS, $m/z$: 290.06 ($M^+$). Anal. calcd. for $C_{18}H_{10}O_4$: C, 74.48; H, 3.47. Found: C, 74.39; H, 3.45.

**3-(2,4-Dichlorobenzoyl)-2*H*-benzo[*f*]chromen-2-one (Vi).** Yellow crystals, mp 255–256°°C. $^1$H NMR: 7.47 (d, $J$ = 8.4 Hz, 2H, ArH), 7.66–7.69 (m, 2H, ArH), 7.74–7.78 (m, 1H, ArH), 7.87–7.96 (m, 2H, ArH), 8.22 (d, $J$ = 9 Hz, 1H, ArH), 8.28 (d, $J$ = 8.1 Hz, 1H, ArH), 8.83 (s, 1H, ArH); $^{13}$C NMR: 114.2, 115.8, 120.8, 125.1, 126.9, 128.6, 129.4, 129.7, 130.8, 131.4, 131.9, 133.3, 134.6, 136.1, 137.5, 139.4, 149.7, 190.1; IR: 1280, 1579, 1664, 3028; MS, $m/z$; 350 ($M^+$). Anal. calcd. for $C_{20}H_{10}Cl_2O_3$: C, 65.06; H, 2.73. Found: C, 65.49; H, 2.61.

### *Biology*

Antimicrobial effects of compounds (**IIIa–i**) and (**Va–i**) were visualized in bioassays using selected microorganisms as test organisms.

**Test microorganisms.** The microorganisms used in the bioassays were purchased from the Institute of Microbial Technology (IMTECH), Chandigarh, India. Two bacteria namely, *Staphylococcus aureus* (MTCC-7443) and *Escherichia coli* (MTCC-725), and two fungal species, namely *Curvularia lunata* (MTCC-2605) and *Fusarium moniliforme* (MTCC-278), were used for the study. Bacterial strains were inoculated on Mueller Hinton agar (MHA) and incubated at 37°C for 24 h. The fungal strains were inoculated on potato dextrose agar (PDA) and incubated at 30°C. Besides, the antimicrobial activity of the compounds was compared with standard antibiotic (streptomycin) and fungicide (fluconazole).

**Antifungal bioassay.** Poison food technique [18, 19] (Grover and Moore, 1962, Mohana and Raversha, 2007) was used for an in vitro study of antifungal activities. The effect of different concentrations of coumarins on the radial growth of test fungi *C. lunata* and *F. moniliforme* were assessed by amending the compounds in potato dextrose agar (PDA) medium. Stock solutions of tested compounds were prepared in acetone (10 mg/mL). Each compound was added to the molten sterilized PDA medium in conical flasks separately to get a final concentration of 100, 200, and 500 μg/mL, respectively. Each PDA medium (25 mL) containing the compounds of the three different concentrations was mixed thoroughly and poured into 90 mm Petri plate. Petri plate without any chemical compounds served as control. In each case, three replicates were taken. PDA containing fluconazole at a concentration of 200 μg/mL served as a standard antifungal agent. The Petri plates after solidification were inoculated separately with mycelial disc (9 mm) of test fungus taken from 4-days pure cultures aseptically and incubated at 37°C in B.O.D incubator till the mycelial growth in the control reached the maximum growth. The radial growth of the test fungus recorded after 5 days by measuring the colony diameter, in comparison with the control, were taken as a measure of fungitoxicity. All the tests were performed in triplicate and the average was taken as final reading.

**Antibacterial bioassay.** The antibacterial assay was assessed by agar well diffusion method using 20 mL of sterile MHA for testing the bacterial activity [20] (Perez et al, 1990). Standard inoculums ($10^6$ CFU/mL) were introduced onto the surface of the sterile agar plates, and a sterile glass spreader was used for even distribution of the inoculums.

Sterile 8-mm diameter cork borers were pierced in the agar in each plate. The stock solution of each chemical was prepared by dissolving 10 mg in 1 mL of acetone. From this stock solution, serial dilutions of the compounds (500, 200, and 100 μg/mL) were prepared. Then the well in each plate was inoculated with the test compound with varying concentrations. Streptomycin (5 mg/mL) was used as positive control and acetone as negative control. The plates were incubated for 24 h at 37°C and the antimicrobial activity was assessed by measuring the diameter of the inhibition zone around the well. All the tests were performed in triplicate and the average was taken as final reading.

## CONCLUSIONS

Compounds (**IIIg**) and (**Ve**) exhibited excellent antifungal activity against the test fungi *Curvularia lunata* and *Fusarium moniliforme*. Highest antibacterial activity against the test bacteria *Escherichia coli* and *Staphylococcus aureus* was shown by compound (**Vd**). The results of antimicrobial screening of the organic compounds lead to the conclusion that the compounds (**IIIg**), (**Vd**), and (**Ve**) are promising antimicrobial drug candidates.

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