Indian Journal of Chemistry
Vol. 64, June 2025, pp. 619-626
DOI: 10.56042/ijc.v64i6.16492

Synthesis, characterization and antibacterial study of novel 2-((*E*)-2-(thiophen-2-yl)vinyl)-4*H*-chromen-4-ones

R S Endait

P.G. Department of Chemistry, Radhabai Kale Mahila Mahavidyalaya, Ahmednagar 414 001, India
E-mail: rupaliendait@gmail.com

Received 17 January 2025; accepted (revised) 28 May 2025

A new series of 2-((*E*)-2-(thiophen-2-yl)vinyl)-4*H*-chromen-4-ones have been synthesized and characterized by mass, IR, ^{1}H and ^{13}C NMR spectroscopy. The characterization data supports the formation of synthesized compounds. All the synthesized compounds have been investigated for antibacterial activity against *Pseudomonas flurescence* (NCIM 2059), *Escherichia coli* (NCIM 2576) as Gram negative and *Staphylococcus aureus* (NCIM 2602), *Bacillus subtilis* (NCIM 2162) as Gram positive bacteria at different concentrations and they show moderate to good antibacterial activity.

Keywords: Thiophene, 1,3-Diketones, Styrylchromones, Antibacterial activity

Due to biological importance of flavones, chemists take good efforts for synthesis of their novel derivatives. Position and nature of substituents decides potential of biological activities associated with flavones. Thiophene and its derivatives attract researchers attention due to its diversified activities as well as importance in medicinal field. It acts as a key building block in different pharmaceuticals and agrochemicals. Thiophene is five membered cyclic heteroaromatic compound.

Thiophene containing derivatives possesses various activities like anticancer[1], antihistamine[2], antitubercular[3,4], antiinflammatory[5], antibacterial[6], antidepressant[7], analgesic[7], 5-ht$_1$a receptor antagonist[8], 5-ht$_6$ receptor antagonist[9], phosphodiesterase-iv inhibitors[10], anti-convulsant[11], *etc*. Thiophene derivatives are also used in the synthesis of pesticides, dyes, petroleum or coal derivatives. There are many pharmaceutical agents having thiophene such as Sufentanil (analgesic agent), Tienilic acid (diuretic agent), Tenoxicam (anti-inflammatory agent), Ethaboxam (fungicide), Dimethenamide (herbicide), *etc*. According to literature study thiophene is present in different structural forms like thienopyridine[12], benzothiophene[13], thienopyrimidine[14], bithienyl[15] showing different biological activities.

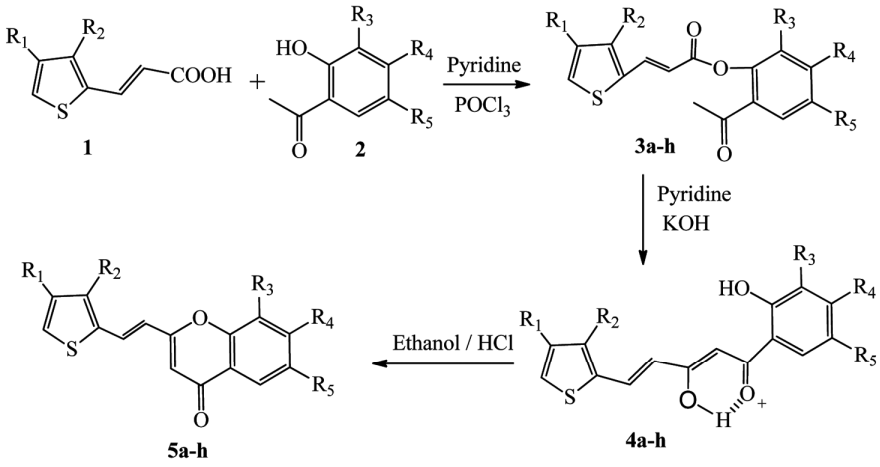
1,3-Diketone is an active intermediate for the organic synthesis. They show metal chelation[16] as well as corrosion inhibitor[17] properties. β-Diketone and its derivatives possess many biological activities like antimicrobial[18,19], HIV-1 integrase inhibitors[20,21], anticarcinogenic[22] and antioxidant[23].

Chromone structure basically found in Flavones and 2-styrylchromones. Isoflavones are present in various plant species while 2-styrylchromones are vinyl analogues and present in a small group of naturally occurring chromones. Synthetic 2-styrylchromones and their derivatives exhibit various biomedicinal activities such as antiviral[24-26], anticancer[27], antioxidant[28,29], antimitotic[30], anti-inflammatory[31], antimicrobial[32], xanthine oxidase inhibitors[33], cytotoxic[34], antiallergic[35], monoamine oxidase B inhibitors[36], antiproliferative agent[37], antimitotic agent[38], anti-rhinovirus[39], anti-norovirus[40], inhibitors of α-amylase and α-glucosidase enzymes[41], β-amyloid imaging agents[42], as well as show affinity and selectivity for A3 adenosine receptors[43].

Keeping in mind the biological activities associated with chromones, in present study we have synthesized thiophene containing substituted chromones (Scheme 1) along with the evaluation of their antibacterial potential.

Experimental Section

All the reagents and solvents were of A. R. grade and used without further purification. Reactions were monitored using thin-layer chromatography (TLC) carried out on pre-coated silica plates. The spot visualization was carried out under UV light. Physical constants were recorded in liquid paraffin bath with the help of capillaries and are uncorrected. The IR spectra of synthesized compounds were recorded on *Shimadzu* IR Affinity-1S Fourier Transform Infrared



Compd 3a, 4a, 5a: R_1, R_3, R_4= H; R_2, R_5=Br
Compd 3b, 4b, 5b: R_1 = Br; R_2, R_3, R_4= H; R_5= Cl
Compd 3c, 4c, 5c: R_1 = Br; R_2, R_3, R_4= H; R_5= Br
Compd 3d, 4d, 5d: R_1 = Br; R_2, R_3= H; R_4= CH_3, R_5= Cl
Compd 3e, 4e, 5e: R_1 = Br; R_2, R_3, R_4= H; R_5= CH_3
Compd 3f, 4f, 5f: R_1, R_4= H, R_2= Br, R_3, R_5=Cl
Compd 3g, 4g, 5g: R_1, R_3 = H; R_2= Br, R_4= CH_3, R_5= Cl
Compd 3h, 4h, 5h: R_1= Br, R_2, R_4= H, R_3, R_5=Cl

Scheme 1 — Reaction scheme of synthesis of 2-((*E*)-2-(thiophen-2-yl)vinyl)-4*H*-chromen-4-ones (**5**)

Spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra of some selected synthesized compounds were recorded on Bruker Avance II 400 MHz NMR spectrometer with DMSO-d_6 as a solvent and TMS as an internal standard. Peak values are shown in δ (ppm). Mass spectra were recorded on Water Acquity TQD mass spectrometer. The biological activities of all synthesized compounds were carried out by using Well Diffusion Method. Gram-negative bacterial strains *Pseudomonas flurescence* (NCIM 2059), *Escherichia coli* (NCIM 2576) and Gram-positive bacteria strains *Staphylococcus aureus* (NCIM 2602), *Bacillus subtilis* (NCIM 2162) were obtained from NCIM (NCL, Pune) and were grown in Luria Burtony medium from Hi Media, India. For the said screening Ampicillin was used as a standard drug. Antibacterial activity was tested against the said strains at concentrations of 100, 30 and 10 μg/mL.

Results and Discussion

Synthesis of 2-((*E*)-2-(thiophen-2-yl)vinyl)-4*H*-chromen-4-ones (**5**) *via* ester was carried out by known method[44]. The reaction is outlined in Scheme 1, where (*E*)-3-(Thiophen-2-yl)acrylic acid **1** on esterification with substituted 2-hydroxy acetophenone **2** gave (*E*)-2-acetylphenyl 3-(thiophen-2-yl)acrylates **3a-h**. IR spectra of **3a** showed the band at 1735 cm^{-1} for –O-C=O frequency. It also exhibited the bands at 1674 and 1614 cm^{-1} for C=O and C=C stretching frequencies respectively. The ^{1}H NMR spectrum of **3a** showed the doublet at δ 6.62 with J = 16 Hz is due to olefinic proton. Singlet at δ 2.51 was due to –CH_3 protons. The mass spectrum of compound **3a** showed the molecular ion peak at *m/z* 430 $[M-H]^+$, along with two isotopic peaks 432 (M+2) and 433.3 (M+4). Compound **3** in basic medium gave 1,3-diketones **4a-h**. IR spectra of **4a** showed the band at 3115 cm^{-1} for –OH stretching frequency. The bands appeared at 1612, 1564 cm^{-1} were due to C=O and C=C stretching frequencies respectively. The ^{1}H NMR spectrum of **4a** showed two –OH singlet's proving keto-enol tautomerism in diketone at δ 15.30 and δ 11.49. The mass spectrum of **4a** showed molecular ion peak at *m/z* 427 $[M-H]^+$ with isotopic peaks 429 (M+2) and 431 (M+4). Intramolecular cyclization of **4a** in acidic medium gave 2-((*E*)-2-(thiophen-2-yl)vinyl)-4*H*-chromen-4-one **5a-h**. IR spectra of **5a** showed the band at 1651 cm^{-1} due to carbonyl. The band at 1620 cm^{-1} indicated C=C stretching frequency. Absence of –OH band in **5a** confirmed the formation of styrylchromones. The ^{1}H NMR spectrum of **5a** showed the singlet at δ 6.47 due to chromone proton. The molecular ion peak of **5a**

was observed at *m/z* 411 $[M+H]^+$ with isotopic peaks 413 (M+2) and 415 (M+4). All these spectral data confirmed the transformation of ester to diketone and to styrylchromone derivatives. The synthesized compounds were also confirmed by ^{13}C NMR spectroscopy and mass spectrometry.

Antibacterial screening

In vitro antibacterial screening of all the synthesized compounds was done by using Well Diffusion Method. Antibacterial activity was tested against *Pseudomonas flurescence* (NCIM 2059), *Escherichia coli* (NCIM 2576) as Gram negative and *Staphylococcus aureus* (NCIM 2602), *Bacillus subtilis* (NCIM 2162) as Gram positive bacteria at concentrations of 100, 30 and 10 µg/mL. Ampicillin was used as a standard drug.

Bacterial strains were obtained from NCIM (NCL, Pune) and were grown in Luria Burtony medium from Hi Media, India. All bacterial cultures were first grown in Luria Burtony media at 37°C at 180 rpm. Once the culture reaches 1 O D it is used for antibacterial assay. The assay was performed in 96 well plates after 8 h and 12 h for Gram negative and Gram positive bacteria respectively[45]. 0.1% of 1 O D culture at 620 nm was used for screening inoculated culture, was added into each well of 96 well plates containing the compounds to be tested. Optical density for each plate was measured at 620 nm after 8 h for Gram negative bacteria and after 12 h for Gram positive bacteria. The *in vitro* preliminary screening values (% inhibition) against micro-organisms tested are summarized in Table 1. The results showed that **3f** exhibited better activity and **5a** moderate activity against *E. coli* at concentration 100 µg/mL. Compounds **3h, 5e** and **5g** showed better activity towards *B. subtilis* while **4h**, **5a** exhibited moderate activity at concentration 100 µg/mL. None of the compounds shows activity against *S. aureus*. Remaining compounds were found to be weakly active or inactive against all four bacterial strains (Table 1).

General procedure for the synthesis of (*E*)-2-acetylphenyl 3-(thiophen-2-yl)acrylate, 3a-h

A mixture of (*E*)-3-(Thiophen-2-yl)acrylic acid **1** (0.01 mol) and substituted 2-hydroxy acetophenone **2** (0.01 mol) was dissolved in 10 mL dry pyridine and it

Table 1 — Antibacterial screening of compounds (% inhibition) **3a-h**, **4a-h**, **5a-h**

Concentration in µg/mL

	Gram Negative Bacteria						Gram Positive Bacteria					
	P. flurescence			*E. coli*			*S. aureus*			*B. subtilis*		
Compd	100	30	10	100	30	10	100	30	10	100	30	10
3a	–	–	–	–	–	–	–	–	–	–	–	–
3b	10.4	7.7	6.3	47.5	4.0	0.5	–	–	–	–	–	–
3c	11.8	11.3	9.6	–	–	–	–	–	–	19.3	–	–
3d	–	–	–	29.7	1.6	0.3	–	–	–	34.8	14.5	10.3
3e	–	–	–	–	–	–	–	–	–	16.3	10.7	1.8
3f	–	–	–	83.5	1.8	–	–	–	–	3.7	3.3	1.0
3g	–	–	–	6.1	–	–	–	–	–	22.1	7.7	–
3h	–	–	–	41.9	9.2	5.2	–	–	–	90.7	19.5	10.0
4a	–	–	–	1.6	–	–	–	–	–	19.8	–	–
4b	–	–	–	32.1	5.0	–	–	–	–	8.6	5.8	4.9
4c	–	–	–	8.9	–	–	–	–	–	6.3	–	–
4d	–	–	–	–	–	–	–	–	–	24.7	13.0	3.7
4e	–	–	–	38.9	28.0	26.8	–	–	–	3.8	–	–
4f	–	–	–	44.1	23.7	23.6	–	–	–	–	–	–
4g	–	–	–	10.4	6.0	–	–	–	–	9.8	4.7	–
4h	–	–	–	20.9	13.3	–	–	–	–	66.9	18.0	8.6
5a	–	–	–	63.3	–	–	–	–	–	79.3	68.9	59.1
5b	–	–	–	–	–	–	–	–	–	10.0	–	–
5c	–	–	–	–	–	–	–	–	–	–	–	–
5d	–	–	–	–	–	–	–	–	–	–	–	–
5e	–	–	–	–	–	–	–	–	–	97.1	25	–
5f	–	–	–	–	–	–	–	–	–	–	–	–
5g	–	–	–	–	–	–	–	–	–	96.6	93.7	42.4
5h	–	–	–	–	–	–	–	–	–	–	–	–
AMP	97.0	95.2	92.2	96.6	92.0	92.1	95.0	93.8	91.1	98.5	95.0	90.5

AMP- Ampicillin, (–) indicates inactive

was cooled to 0°C in ice bath. To this reaction mixture 0.01 mol of $POCl_3$ was added with stirring while maintaining the temperature below 5°C. After complete addition of $POCl_3$, the reaction mixture was kept overnight at RT and then poured over crushed ice. The product was purified by recrystallization from alcohol to afford compound **3**.

(*E*)-2-Acetyl-4-bromophenyl 3-(3-bromothiophen-2-yl)acrylate, 3a: Off White solid. Yield 65%. m. p. 104-106°C. IR: 1735 (-O-C=O), 1674 (C=O), 1614 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.51 (s, 3H, CH_3), 6.62 (d, 1H, =CH, *J*= 16.0 Hz), 7.29 (m, 2H, Ar-H), 7.80-7.84 (m, 2H, Ar-H & =CH), 7.94 (d, 1H, Ar-H, *J*= 4.0 Hz), 8.05 (d, 1H, Ar-H, *J*= 2.4 Hz); ^{13}C NMR ($CDCl_3$): δ 29.79, 116.68, 117.51, 119.29, 125.54, 128.95, 131.78, 132.87, 132.89, 133.81, 136.05, 138.04, 148.04, 164.36, 196.26; MS: *m/z* 430 $[M-H]^+$, 432 (M+2), 433.3 (M+4).

(*E*)-2-Acetyl-4-chlorophenyl 3-(4-bromothiophen-2-yl)acrylate, 3b: Off White solid. Yield 62%. m. p. 109-110°C. IR: 1741 (-O-C=O), 1680 (C=O), 1622 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.42 (s, 3H, CH_3), 6.67 (d, 1H, =CH, *J*= 16.01 Hz), 7.36 (d, 1H, Ar-H, *J*= 8.0 Hz), 7.64 (s, 1H, Ar-H), 7.86-7.90 (m, 2H, Ar-H & =CH), 7.92 (s, 1H, Ar-H), 8.06 (d, 1H, Ar-H, *J*= 2.4 Hz); ^{13}C NMR ($CDCl_3$): δ 29.78, 116.63, 117.50, 119.28, 125.52, 128.96, 131.77, 132.86, 132.88, 133.82, 136.04, 138.06, 148.00, 164.36, 196.26; MS: *m/z* 384 $[M-H]^+$, with isotopic peak.

(*E*)-2-Acetyl-4-bromophenyl 3-(4-bromothiophen-2-yl)acrylate, 3c: Off White solid. Yield 59%. m. p. 110-112°C. IR: 1733 (-O-C=O), 1675 (C=O), 1610 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.49 (s, 3H, CH_3), 6.65 (d, 1H, =CH, *J*= 15.9 Hz), 7.27 (d, 1H, Ar-H, *J*= 8.2 Hz), 7.82-7.87 (m, 2H, Ar-H & =CH), 7.68 (s, 1H, Ar-H), 7.96 (s, 1H, Ar-H), 8.03 (d, 1H, Ar-H, *J*= 2.2 Hz); ^{13}C NMR ($CDCl_3$): δ 29.75, 116.69, 117.52, 119.29, 125.55, 128.94, 131.79, 132.88, 132.90, 133.81, 136.06, 138.03, 148.02, 164.38, 196.25; MS: *m/z* 428 $[M-H]^+$, with isotopic peak.

(*E*)-2-Acetyl-4-chloro-5-methylphenyl 3-(4-bromothiophen-2-yl)acrylate, 3d: Off White solid. Yield 68%. m. p. 122-124°C. IR: 1740 (-O-C=O), 1679 (C=O), 1620 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.30 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 6.64 (d, 1H, =CH, *J*= 16.02 Hz), 7.35 (s, 1H, Ar-H), 7.66 (s, 1H, Ar-H), 7.82 (s, 1H, =CH), 7.95 (s, 1H, Ar-H), 8.08 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 20.02, 29.77, 116.70, 117.49, 119.27, 125.53, 128.95, 131.78, 132.86, 132.92, 133.84, 136.03, 138.05, 148.03, 164.37, 196.27; MS: *m/z* 398 $[M-H]^+$, with isotopic peak.

(*E*)-2-Acetyl-4-methylphenyl 3-(4-bromothiophen-2-yl)acrylate, 3e: Off White solid. Yield 67%. m. p. 114-115°C. IR: 1738 (-O-C=O), 1677 (C=O), 1619 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.34 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 6.56 (d, 1H, =CH, *J*= 15.98 Hz), 7.38 (d, 1H, Ar-H, *J*= 8.01 Hz), 7.65 (s, 1H, Ar-H), 7.80-7.85 (m, 2H, Ar-H & =CH), 7.90 (s, 1H, Ar-H), 8.01 (d, 1H, Ar-H, *J*= 2.4 Hz); ^{13}C NMR ($CDCl_3$): δ 23.21, 29.79, 116.60, 117.45, 119.25, 125.50, 128.90, 131.70, 132.81, 132.91, 133.77, 136.11, 138.08, 148.09, 164.30, 196.20; MS: *m/z* 364 $[M-H]^+$, with isotopic peak.

(*E*)-2-Acetyl-4,6-dichlorophenyl 3-(3-bromothiophen-2-yl)acrylate, 3f: Off White solid. Yield 60%. m. p. 110-111°C. IR: 1735 (-O-C=O), 1674 (C=O), 1614 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.54 (s, 3H, CH_3), 6.57 (d, 1H, =CH, *J*= 15.68 Hz), 7.21 (d, 1H, Ar-H, *J*= 4.0 Hz), 7.80-7.86 (m, 3H, Ar-H & =CH), 7.95 (d, 1H, =CH, *J*= 15.7 Hz); ^{13}C NMR ($CDCl_3$): δ 29.82, 116.62, 117.46, 119.21, 125.51, 128.91, 131.72, 132.80, 132.90, 133.74, 136.10, 138.09, 148.10, 164.32, 196.28; MS: *m/z* 417 $[M-H]^+$, with isotopic peak.

(*E*)-2-Acetyl-4-chloro-5-methylphenyl 3-(3-bromothiophen-2-yl)acrylate, 3g: Off White solid. Yield 63%. m. p. 128-130°C. IR: 1737 (-O-C=O), 1678 (C=O), 1617 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.37 (s, 3H, CH_3), 2.70 (s, 3H, CH_3), 6.63 (d, 1H, =CH, *J*= 16 Hz), 7.25 (s, 1H, Ar-H), 7.78-7.83 (m, 2H, Ar-H & =CH), 7.96 (s, 1H, Ar-H), 8.06 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 20.05, 29.76, 116.71, 117.50, 119.26, 125.53, 128.95, 131.77, 132.85, 132.93, 133.83, 136.04, 138.05, 148.03, 164.37, 196.27; MS: *m/z* 398 $[M-H]^+$, with isotopic peak.

(*E*)-2-Acetyl-4,6-dichlorophenyl 3-(4-bromothiophen-2-yl)acrylate, 3h: Off White solid. Yield 64%. m. p. 119-120°C. IR: 1736 (-O-C=O), 1673 (C=O), 1615 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.50 (s, 3H, CH_3), 6.54 (d, 1H, =CH, *J*= 15.7 Hz), 7.62 (s, 1H, Ar-H), 7.81-7.88 (m, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 8.08 (d, 1H, Ar-H, J= 2.3 Hz); ^{13}C NMR ($CDCl_3$): δ 29.81, 116.61, 117.47, 119.22, 125.50,

128.90, 131.73, 132.79, 130.91, 133.73, 136.08, 138.10, 148.10, 164.32, 196.28; MS: *m/z* 418 $[M-H]^+$, with isotopic peak.

General procedure for the synthesis of (*E*)-1-(2-hydroxyphenyl)-5-(thiophen-2-yl)pent-4-ene-1,3-dione, 4a-h:

Compound **3** (0.02 mol) was taken in 15 mL dry pyridine, to this reaction mixture powdered KOH (1 gm) was added with constant stirring. After addition of KOH the reaction mixture was stirred at RT for 3 hrs on the magnetic stirrer. Then the contents were poured over crushed ice and acidified with dil. HCl. The product was separated by filtration and purified by recrystallization from ethanol to yield compound **4**.

(2*Z*,4*E*)-1-(5-Bromo-2-hydroxyphenyl)-5-(3-bromothiophen-2-yl)-3-hydroxypenta-2,4-dien-1-one, 4a: Yellow solid. Yield 61%. m. p. 158-159°C. IR: 3115 (-OH), 1612 (C=O), 1564 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.79 (d, 1H, =CH, *J*= 16.0 Hz), 6.95-6.98 (m, 2H, Ar-H), 7.27 (d, 1H, Ar-H, *J*= 8.0 Hz), 7.60-7.67 (m, 2H, Ar-H), 7.88 (d, 1H, Ar-H, *J*= 4.8 Hz), 7.98 (d, 1H, Ar-H, *J*= 2.4 Hz), 11.49 (s, 1H, phenolic -OH), 15.30 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 97.15, 110.77, 111.37, 120.35, 120.76, 122.05, 125.44, 130.74, 131.60, 132.38, 138.44, 141.11, 161.55, 174.07, 194.64; MS: *m/z* 427 $[M-H]^+$, 429 (M+2), 431 (M+4).

(2*Z*,4*E*)-5-(4-Bromothiophen-2-yl)-1-(5-chloro-2-hydroxyphenyl)-3-hydroxypenta-2,4-dien-1-one, 4b: Yellow solid. Yield 59%. m. p. 174-176°C. IR: 3115 (-OH), 1615 (C=O), 1561 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.77 (d, 1H, =CH, *J*= 16.0 Hz), 6.99 (s, 1H, =CH), 7.29 (d, 1H, Ar-H, *J*= 8.1 Hz), 7.63-7.71 (m, 2H, Ar-H), 7.79 (s, 1H, Ar-H), 7.86 (s, 1H, Ar-H), 8.06 (d, 1H, Ar-H, *J*= 2.4 Hz), 11.21 (s, 1H, phenolic -OH), 15.22 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 97.14, 110.73, 111.30, 120.35, 120.77, 122.06, 125.43, 130.73, 131.61, 132.36, 138.40, 141.12, 161.54, 174.06, 194.62; MS: *m/z* 385 $[M-H]^+$, with isotopic peak.

(2*Z*,4*E*)-1-(5-Bromo-2-hydroxyphenyl)-5-(4-bromothiophen-2-yl)-3-hydroxypenta-2,4-dien-1-one, 4c: Yellow solid. Yield 57%. m. p. 150-152°C. IR: 3118 (-OH), 1617 (C=O), 1571 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.74 (d, 1H, Ar-H, *J*= 16.02 Hz), 6.91 (s, 1H, =CH), 7.37 (d, 1H, Ar-H, *J*= 8.1 Hz), 7.61-7.70 (m, 2H, Ar-H), 7.78 (s, 1H, Ar-H), 7.87 (s, 1H, Ar-H), 8.08 (d, 1H, Ar-H, *J*= 2.2 Hz), 11.24 (s, 1H, phenolic -OH), 15.20 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 97.18, 110.70, 111.29, 120.34, 120.75, 122.04, 125.42, 130.72, 131.58, 132.36, 138.42, 141.10, 161.53, 174.05, 194.60; MS: *m/z* 427 $[M-H]^+$, with isotopic peak.

(2*Z*,4*E*)-5-(4-Bromothiophen-2-yl)-1-(5-chloro-2-hydroxy-4-methylphenyl)-3-hydroxypenta-2,4-dien-1-one, 4d: Yellow solid. Yield 64%. m. p. 229-230°C. IR: 3120 (-OH), 1618 (C=O), 1569 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.42 (s, 3H, CH_3), 6.75 (d, 1H, =CH, *J*= 15.99 Hz), 6.98 (s, 1H, =CH), 7.54 (s, 1H, =CH), 7.62 (s, 1H, Ar-H), 7.82 (s, 1H, ArH), 7.91 (s, 1H, Ar-H), 8.05 (s, 1H, Ar-H), 11.22 (s, 1H, phenolic -OH), 15.14 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 23.25, 97.18, 110.78, 111.28, 120.31, 120.72, 122.01, 125.40, 130.71, 131.59, 132.37, 138.41, 141.14, 161.58, 174.09, 194.66; MS: *m/z* 399 $[M-H]^+$, with isotopic peak.

(2*Z*,4*E*)-5-(4-Bromothiophen-2-yl)-3-hydroxy-1-(2-hydroxy-5-methylphenyl)penta-2,4-dien-1-one, 4e: Yellow solid. Yield 63%. m. p. 158-160°C. IR: 3114 (-OH), 1611 (C=O), 1565 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.35 (s, 3H, CH_3), 6.73 (d, 1H, Ar-H, *J*= 15.5 Hz), 6.96 (s, 1H, =CH), 7.32 (d, 1H, Ar-H, *J*= 8.0 Hz), 7.58-7.67 (m, 2H, Ar-H), 7.82 (s, 1H, Ar-H), 7.85 (s, 1H, Ar-H), 8.07 (d, 1H, Ar-H, *J*= 2.6 Hz), 11.29 (s, 1H, phenolic -OH), 15.10 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 23.15, 97.17, 110.72, 111.31, 120.32, 120.73, 122.01, 125.42, 130.76, 131.58, 132.36, 138.42, 141.09, 161.53, 174.03, 194.60; MS: *m/z* 365 $[M-H]^+$, with isotopic peak.

(2*Z*,4*E*)-5-(3-Bromothiophen-2-yl)-1-(3,5-dichloro-2-hydroxyphenyl)-3-hydroxypenta-2,4-dien-1-one, 4f: Yellow solid. Yield 58%. m. p. 195-196°C. IR: 3116 (-OH), 1613 (C=O), 1568 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.72 (d, 1H, =CH, *J*= 14.96 Hz), 6.94 (s, 1H, =CH), 7.18 (d, 1H, Ar-H, *J*= 5.3 Hz), 7.69-7.75 (m, 2H, Ar-H), 7.97 (s, 1H, Ar-H), 8.14 (s, 1H, Ar-H), 12.64 (s, 1H, phenolic -OH), 15.25 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 97.15, 110.73, 111.32, 120.33, 120.70, 122.00, 125.40, 130.72, 131.60, 132.35, 138.41, 141.11, 161.53, 174.04, 194.61; MS: *m/z* 418 $[M-H]^+$, with isotopic peak.

(2*Z*,4*E*)-5-(3-Bromothiophen-2-yl)-1-(5-chloro-2-hydroxy-4-methylphenyl)-3-hydroxypenta-2,4-dien-1-one, 4g: Yellow solid. Yield 56%. m. p. 162-163°C. IR: 3113 (-OH), 1610 (C=O), 1566 (C=C) cm^{-1};

^{1}H NMR (DMSO-d_6): δ 2.41 (s, 3H, CH_3), 6.77 (d, 1H, =CH, *J*= 16.0 Hz), 6.92-6.97 (m, 2H, Ar-H & =CH), 7.56 (s, 1H, Ar-H), 7.68 (s, 1H, Ar-H), 7.91 (s, 1H, Ar-H), 8.03 (s, 1H, Ar-H), 11.32 (s, 1H, phenolic -OH), 15.15 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 23.20, 97.18, 110.80, 111.34, 120.35, 120.74, 122.03, 125.44, 130.74, 131.62, 132.37, 138.43, 141.14, 161.54, 174.06, 194.62; MS: *m/z* 399 $[M-H]^+$, with isotopic peak.

(2*Z*,4*E*)-5-(4-Bromothiophen-2-yl)-1-(3,5-dichloro-2-hydroxyphenyl)-3-hydroxypenta-2,4-dien-1-one, 4h: Yellow solid. Yield 60%. m. p. 168-169°C. IR: 3122 (-OH), 1619 (C=O), 1571 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.68 (d, 1H, =CH, *J*= 14.94 Hz), 6.84 (s, 1H, =CH), 7.67 (d, 1H, =CH, *J*= 15.99 Hz), 7.79 (d, 1H, Ar-H, *J*= 2.4 Hz), 7.81 (s, 1H, Ar-H), 7.86 (s, 1H, Ar-H), 8.09 (s, 1H, Ar-H), 12.31 (s, 1H, phenolic -OH), 15.11 (s, 1H, enolic -OH); ^{13}C NMR ($CDCl_3$): δ 97.21, 110.82, 111.37, 120.38, 120.76, 122.04, 125.38, 130.76, 131.61, 132.35, 138.40, 141.15, 161.56, 174.08, 194.60; MS: *m/z* 419 $[M-H]^+$, with isotopic peak.

Synthesis of 2-((*E*)-2-(thiophen-2-yl)vinyl)-4*H*-chromen-4-one, 5a-h:

Compound **4** was taken in 10 mL ethanol and to this 1 mL conc. HCl was added. Reaction mixture was heated under reflux for 3 hrs. After completion of reaction (checked by TLC), the reaction mixture was cooled and poured over crushed ice. The product was separated by filtration and purified by recrystallization from ethanol to yield compound **5**.

(*E*)-6-Bromo-2-(2-(3-bromothiophen-2-yl)vinyl)-4*H*-chromen-4-one, 5a: White solid. Yield 58%. m. p. 176-178°C. IR: 1651 (C=O), 1620 (C=C), 1274 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.47 (s, 1H, chromone), 6.86 (d, 1H, =CH, *J*= 16.0 Hz), 7.13 (d, 1H, Ar-H, *J*= 5.3 Hz), 7.60-7.71 (m, 3H, Ar-H), 7.86 (dd, 1H, Ar-H, *J*= 2.4 & 8.8 Hz), 8.12 (d, 1H, Ar-H, *J*= 2.4 Hz); ^{13}C NMR ($CDCl_3$): δ 110.75, 115.49, 118.55, 119.91, 120.55, 125.45, 127.53, 128.22, 128.38, 131.59, 134.93, 136.72, 154.71, 161.24, 176.85; MS: *m/z* 411 $[M+H]^+$, 413 (M+2) and 415 (M+4).

(*E*)-2-(2-(4-Bromothiophen-2-yl)vinyl)-6-chloro-4*H*-chromen-4-one, 5b: White solid. Yield 55%. m. p. 184-185°C. IR: 1656 (C=O), 1619 (C=C), 1270 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.45 (s, 1H, chromone), 6.84 (d, 1H, =CH, *J*= 16.02 Hz), 7.63 (d, 1H, =CH, *J*= 16.00 Hz), 7.72 (d, 1H, Ar-H, *J*= 8.8 Hz), 7.78 (dd, 1H, Ar-H, *J*= 2.8 & 8.8 Hz), 7.87 (s, 1H, Ar-H), 7.95 (s, 1H, Ar-H), 8.16 (d, 1H, Ar-H, *J*= 2.8 Hz); ^{13}C NMR ($CDCl_3$): δ 110.76, 115.48, 118.56, 119.92, 120.56, 125.44, 127.50, 128.24, 128.39, 131.58, 134.94, 136.73, 154.72, 161.25, 176.83; MS: *m/z* 367 $[M+H]^+$ with isotopic peak.

(*E*)-6-Bromo-2-(2-(4-bromothiophen-2-yl)vinyl)-4*H*-chromen-4-one, 5c: White solid. Yield 53%. m. p. 196-197°C. IR: 1652 (C=O), 1621 (C=C), 1271 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.47 (s, 1H, chromone), 6.89 (d, 1H, =CH, *J*= 16.0 Hz), 7.62-7.74 (m, 2H, Ar-H & =CH), 7.84 (s, 1H, Ar-H), 7.89 (dd, 1H, Ar-H, *J*= 2.4 & 8.2 Hz), 7.96 (s, 1H, Ar-H), 8.15 (d, 1H, Ar-H, *J*= 2.4 Hz); ^{13}C NMR ($CDCl_3$): δ 110.77, 115.47, 118.53, 119.90, 120.53, 125.46, 127.53, 128.23, 128.40, 131.60, 134.92, 136.74, 154.70, 161.23, 176.82: MS: *m/z* 411 $[M+H]^+$, with isotopic peak.

(*E*)-2-(2-(4-Bromothiophen-2-yl)vinyl)-6-chloro-7-methyl-4*H*-chromen-4-one, 5d: White solid. Yield 59%. m. p. 169-172°C. IR: 1654 (C=O), 1625 (C=C), 1275 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.42 (s, 3H, CH_3), 6.48 (s, 1H, chromone), 6.85 (d, 1H, =CH, *J*= 15.96 Hz), 7.62 (s, 1H, =CH), 7.81 (s, 1H, Ar-H), 8.87 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 8.15 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 23.18, 110.74, 115.45, 118.52, 119.89, 120.52, 125.48, 127.55, 128.21, 128.35, 131.57, 134.95, 136.70, 154.73, 161.26, 176.86: MS: *m/z* 381 $[M+H]^+$, with isotopic peak.

(*E*)-2-(2-(4-Bromothiophen-2-yl)vinyl)-6-methyl-4*H*-chromen-4-one, 5e: White solid. Yield 60%. m. p. 170-171°C. IR: 1649 (C=O), 1617 (C=C), 1273 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.38 (s, 3H, CH_3), 6.44 (s, 1H, chromone), 6.87 (d, 1H, =CH, *J*= 16.03 Hz), 7.60-7.72 (m, 2H, Ar-H & =CH), 7.81 (s, 1H, Ar-H), 7.86 (dd, 1H, Ar-H, *J*= 2.2 & 8.0 Hz), 7.94 (s, 1H, Ar-H), 8.11 (d, 1H, Ar-H, *J*= 2.2 Hz); ^{13}C NMR ($CDCl_3$): δ 23.28, 110.73, 115.46, 118.54, 119.92, 120.58, 125.49, 127.52, 128.29, 128.37, 131.61, 134.91, 136.71, 154.69, 161.22, 176.84: MS: *m/z* 347 $[M+H]^+$, with isotopic peak.

(*E*)-2-(2-(3-Bromothiophen-2-yl)vinyl)-6,8-dichloro-4*H*-chromen-4-one, 5f: White solid. Yield 56%. m. p. 210-212°C. IR: 1653 (C=O), 1622 (C=C), 1277 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.41 (s, 1H, chromone), 6.88 (d, 1H, =CH, *J*= 16.0 Hz), 7.17 (d, 1H, Ar-H, *J*= 5.0 Hz), 7.66 (d, 1H, =CH, *J*= 15.95 Hz), 7.89 (d, 1H, Ar-H, *J*= 2.6 Hz), 7.91 (s, 1H, Ar-H), 8.10 (d,

1H, Ar-H, *J*= 2.6 Hz); ^{13}C NMR ($CDCl_3$): δ 110.72, 115.50, 118.56, 119.93, 120.56, 125.47, 127.51, 128.22, 128.36, 131.56, 134.90, 136.72, 154.74, 161.27, 176.85: MS: *m/z* 401 $[M+H]^+$, with isotopic peak.

(*E*)-2-(2-(3-Bromothiophen-2-yl)vinyl)-6-chloro-7-methyl-4*H*-chromen-4-one, 5g: White solid. Yield 54%. m. p. 180-181°C. IR: 1650 (C=O), 1618 (C=C), 1272 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.38 (s, 3H, CH_3), 6.40 (s, 1H, chromone), 6.82 (d, 1H, =CH, *J*= 16.0 Hz), 7.16 (d, 1H, Ar-H, *J*= 5.1 Hz), 7.65 (d, 1H, =CH, *J*= 16.0 Hz), 7.78 (s, 1H, Ar-H), 7.88 (s, 1H, Ar-H), 8.12 (s, 1H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 23.25, 110.79, 115.51, 118.57, 119.94, 120.54, 125.42, 127.54, 128.20, 128.42, 131.62, 134.96, 136.75, 154.68, 161.21, 176.87: MS: *m/z* 381 $[M+H]^+$, with isotopic peak.

(*E*)-2-(2-(4-Bromothiophen-2-yl)vinyl)-6,8-dichloro-4*H*-chromen-4-one, 5h: White solid. Yield 58%. m. p. 176-177°C. IR: 1648 (C=O), 1624 (C=C), 1276 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 6.43 (s, 1H, chromone), 6.87 (d, 1H, =CH, *J*= 16.04 Hz), 7.65 (d, 1H, =CH, *J*= 16.04 Hz), 7.90 (d, 1H, Ar-H, *J*= 2.0 Hz), 7.94 (s, 1H, Ar-H), 7.98 (s, 1H, Ar-H), 8.14 (d, 1H, Ar-H, *J*= 2.0 Hz); ^{13}C NMR ($CDCl_3$): δ 110.71, 115.52, 118.58, 119.89, 120.57, 125.43, 127.49, 128.22, 128.41, 131.57, 134.93, 136.72, 154.74, 161.26, 176.89: MS: *m/z* 401 $[M+H]^+$, with isotopic peak.

Conclusion

In the synthesis of styryl chromones, we found that the compounds with substituents like halogens (Cl, Br) and alkyl groups exhibited prominent antibacterial activity and on further structural modifications they may become potent lead compounds.

Supplementary data

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

Acknowledgements

The author is thankful to the Director, SAIF, Panjab University, Chandigarh for providing spectral information as well as thankful to D. Sarkar and coworkers, NCL, Pune for providing antibacterial screening of synthesized compounds.

References

1 Mostafa M G, Mahmoud S B & Mansour S A, *Acta Pharm*, 64 (2014) 419.
2 Clapp R C, Clark J H, Vaughan J R, English J P & Anderson G W, *J Am Chem Soc*, 69 (1947) 1549.
3 Xiaoyun L, Baojie W, Scott G F & Qidong Y, *Eur J Med Chem*, 46 (2011) 3551.
4 Parai M K, Panda G, Chaturvedi V, Manju Y K & Sinha S, *Bioorg Med Chem Lett,*18 (2008) 289.
5 Pillai A D, Rathod P D, Xavier F P, Vasu K K, Padh H & Sudarsanam V, *Bioorg Med Chem*, 12 (2004) 4667.
6 Khalil A M, Berghot M A & Gouda M A, *Eur J Med Chem*, 44 (2009) 4434.
7 Wardakhan W W, Abdel-salam O M E & Elmegeed G A, *Acta Pharm*, 58 (2008) 1.
8 El-Kerdawy M M, El-Bendary E R, Abdel-Aziz A A M, Elwasseef D R & Abd El-Aziz N I, *Eur J Med Chem*, 45 (2010) 1805.
9 Ivachtchenko A V, Golovina E S, Kadieva M G, Koryakova A G, Kovalenko S M, Mitkin O D, Okun I M, Ravnyeyko I M, Tkachenko S E & Zaremba O V, *Bioorg Med Chem*, 18 (2010) 5282.
10 Cashman J R & Ghirmai S, *Bioorg Med Chem*, 17 (2009) 6890.
11 Jain A K, Vaidya A, Ravichandran V, Kashaw S K & Agrawal R K, *Bioorg Med Chem*, 20 (2012) 3378.
12 Master H E, Khan S I & Poojari K A, *Indian J Chem Sec B,* 47B (2008) 97.
13 Wang J, Yang C, Ding H, Yan X, Wu X & Xie Y, *Indian J Chem Sec B*, 45B (2006) 318.
14 Lagardere P, Fersing C, Masurier N & Lisowski V, *Pharmaceuticals,* 15 (2022) 35.
15 Vasudeva N, Gupta P & Sharma S K, *Ind J Heterocycl Chem*, 16 (2007) 303.
16 Kelin A V, *Curr Org Chem*, 7 (2003) 1691.
17 Lubanski F M, Octavio O X, Marco A D A, Eugenio A F, Paulina A L & Federico J C, *Corrosion Science*, 61 (2012) 171.
18 Korde N S, Gaikwad S T, Khade B C & Rajbhoj A S, *Chem Sci Trans*, 2 (2013) 407.
19 Korde N S, Rajbhoj A S, Gaikwad S T & Khade B C, *World J Pharma Res*, 4 (2015) 1571.
20 Hu L, Li Z, Wang Z, Liu G, He X, Wang X & Zeng C, *Med Chem*, 11 (2015) 180.
21 Pais G C G, Zhang X, Marchand C N, Cowansage K, Svarovskaia E S, Pathak V K, Tang Y, Nicklaus M, Pommier Y & Burke T R, *J Med Chem*, 45 (2002) 3184.
22 Singletary K, MacDonald C, Iovinelli M, Fisher C & Wallig M, *Carcinogenesis*, 19 (1998) 1039.
23 Sugiyama Y, Kawakishi S & Osawa T, *Biochem Pharmacol*, 52 (1996) 519.
24 Desideri N, Mastromarino P & Conti C, *Antivir Chem Chemother*, 14 (2003) 195.
25 Rocha-Pereira J, Cunha R, Pinto D C, Silva A M & Nascimento M S, *Bioorg Med Chem*, 18 (2010) 4195.
26 Conti C, Mastromarino P, Goldoni P, Portalone G & Desideri N, *Antivir Chem Chemother*, 6 (2005) 267.
27 Shaw A Y, Chang C Y, Liau H H, Lu P J, Chen H L, Yang C N & Li H Y, *Eur J Med Chem*, 44 (2009) 2552.
28 Filipe P, Silva A M S, Morliere P, Brito C M, Patterson L K, Hug G L, Silva J N, Cavaleiro A S, Maziere J C, Freitas J P & Santus R, *Bio Chem Pharmacol*, 67 (2004) 2207.
29 Gomes A, Fernandes E, Garcia M B Q, Silva A M S, Pinto D C G A, Santos C M M, Cavaleiro J A S & Lima J L F C, *Bioorg Med Chem*, 16 (2008) 7939.
30 Marinho J, Pedro M, Pinto D C G A, Silva A M S, Cavaleiro J A S, Sunkel C E & Nascimento M S J, *Biochem Pharmacol*, 75 (2008) 826.

31 Gomes A, Fernandes E, Silva A M S, Pinto D C G A, Santos C M M, Cavaleiro J A S & Lima J L F C, *Biochem Pharma*, 78 (2009) 171.

32 Gadhave A, Gaikar R, Kuchekar S & Karale B, *Indian J Chem Sec B*, 54B (2015) 383.

33 Fernandes E, Carvalho F, Silva A M S, Santos C M M, Pinto D C G A, Cavaleiro J A S & Bastos M L, *J Enzyme Inhib Med Chem*, 17 (2002) 45.

34 Vasu K, Harikrishna N, Nagaraju K & Rao C V, *Der Pharma Sinica*, 5 (2014) 40.

35 Doria G, Romeo C, Forgione A, Sberze P, Tibolla N, Corno M L, Cruzzola G & Cadelli G, *Eur J Med Chem Chim Ther*, 14 (1979) 347.

36 Takao K, Endo S, Nagai J, Kamauchi H, Takemura Y, Uesawa Y & Sugita Y, *Bioorg Chem*, 92 (2019) 103285.

37 Shaw A Y, Chang C Y, Liau H H, Lu P J, Chen H L, Yang C N & Li H Y, *Eur J Med Chem*, 44 (2009) 2552.

38 Marinho J, Pedro M, Pinto D C G A, Silva A M S, Cavaleiro J A S, Sunkel C E, Nascimento M S J, *Biochem Pharmacol*, 75 (2008) 826.

39 Desideri N, Conti C, Mastromarino P & Mastropaolo F, *Antivir Chem Chemother*, 11 (2000) 373.

40 Pereira J R, Cunha R, Pinto D C G A, Silva A M S & Nascimento M S J, *Bioorg Med Chem*, 18 (2010) 4195.

41 Santos C M M, Proenca C, Freitas M, Araujo A N, Silva A M S & Fernandes E, *Med Chem Res*, 33 (2024) 600.

42 Ono M, Maya Y, Haratake M & Nakayama M, *Bioorg Med Chem,* 15 (2007) 444.

43 Karton Y, Jiang J L, Ji X D, Melman N, Olah M E, Stiles G L & Jacobson K A, *J Med Chem,* 39 (1996) 2293.

44 Ujwala B, Priyadarsini P & Rao V M, *Int J Pharm Bio Sci*, 4 (2013) 199.

45 Honmore V S, Natu A D, Khedkar V M, Arkile M A, Sarkar D & Rojatkar S R, *Nat Prod Res*, 36 (2022) 2465.