# Synthesis, crystal structure and antitumour activity evaluation of 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives

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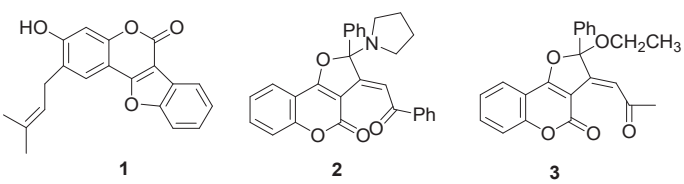
A series of 1*H*-thieno[2,3-c]chromen-4(2*H*)-one derivatives were synthesised through Knoevenagel condensation of substituted flavanones with thiazolidine-2,4-dione in ethanol in the presence of piperidine. The mechanism of the reaction was proposed. All synthesised compounds were characterised by IR, $^1$H NMR, $^{13}$C NMR, HRMS, and elemental analysis. The structure of 2-(3-chlorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one was confirmed by a single crystal X-ray diffraction analysis. A preliminary antitumour screening showed that 2-(2-fluorophenyl)-1*H*-thieno [2,3-*c*]chromen-4(2*H*)-one had moderate to good activity against A549, BGC-823, HCT116 and MDA-MB-453 cancer cell lines, and 2-(3,4-dimethoxyphenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one displayed similar activity against these four kinds of cancer cells compared with the reference drug.

**Keywords:** 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives, Knoevenagel condensation, antitumour activity

Flavanones display important biological activities, including aldose reductase inhibitors and as anticancer, antibacterial and anti-inflammatories.[1–4] They are also used as important intermediates in the synthesis of many biologically active compounds. Studies have shown that thiazolidine-2,4-dione derivatives have a wide variety of biological properties, such as hypoglycemic, anti-inflammatory, anti-atherosclerosis, and antitumour activity.[5–7]

Coumarin derivatives have aroused considerable attention for their broad spectra of bioactivities, such as anti-inflammatory,[8] antimicrobial,[9] antiangiogenic,[10] antinociceptive,[11] anti-HIV,[12] antitumour,[13] and so on. The antitumour activity of natural and synthetic coumarin derivatives has been extensively explored by many researchers, and it had been shown that coumarins, depending on their structures, can act on various tumour cells by different mechanisms.[14]

Szliska *et al.*[15] demonstrated that psoralidin (Fig. 1; **1**) isolated from *Psoralea corylifolia* in combination with TRAIL (tumour necrosis factor related apoptosis inducing ligand) enhanced the potential of TRAIL for inducing apoptosis in sensitised TRAIL-resistant LNCaP (prostate cancer cells). Furocoumarins, coumarin derivatives fused with furan ring, showed a wide range of biological activities.[14] Rajabi *et al.*[16] synthesised furo[3,2-*c*]coumarin derivatives (Fig. 1; **2** and **3**), which showed a very good anticancer activity by cell growth inhibition of the HCT-15 cell line (colon cancer).



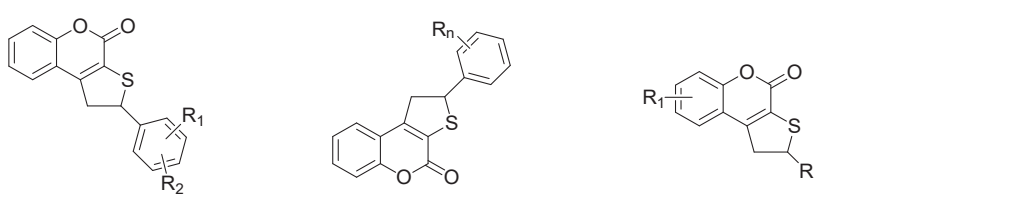

**1** **2** **3**

**Fig. 1** Structures of 2*H*-furo[3,2-*c*]chromen-4(3*H*)-one derivatives.

Manna *et al.*[17] have demonstrated that some dihydrothienocoumarins have potent analgesic and anti-inflammatory activity (Fig. 2; **4**). The relation between conformation and analgesic activity of 2-aryldihydrothienobenzopyranones has been studied by Robert *et al.*[18] (Fig. 2; **5**); Xicluna *et al.*[19] have reported that some dihydrothienocoumarins have analgesic activity, but no anti-inflammatory activity (Fig. 2; **6**); however, few literature references about the antitumour activity of these kinds of compounds were found.

## Results and discussion

Initially, we intended to prepare novel flavanone derivatives bearing the thiazolidine-2,4-dione moiety based on the split principle. However, a series of dihydrothienocoumarins were obtained instead of the desired flavanone derivatives. Intermediates **7** are readily available as shown in Scheme 1 and can be advanced with cyclisation to **8**. We had tried to synthesise the novel flavanone derivatives **9** bearing the thiazolidine-2,4-dione moiety through Knoevenagel condensation of compounds **8**, with thiazolidine-2,4-dione in the presence of piperidine in ethanol. The proposed synthetic pathway is shown in Scheme 1. However when the product was characterised, a single peak of –NH was not shown in the $^1$H NMR spectrum and the value of the molecular ion peak shown in the mass spectrum was 43 less than that of the desired compound **9a**. Moreover, data from the elemental analysis showed that there was no nitrogen atom




($R_1$=H, $R_2$=2-, 3-, 4-Br; $R_1$=2-Cl, $R_2$=4-Cl; $R_1$=2-MeO, $R_2$=4-, 5-MeO) **4**

(R=H, OMe, or Cl; n=1-2) **5**

(R=substituted Ph ;$R_1$ =H, $NO_2$, Me, Cl, NHAc) **6**

**Fig. 2** Structures of 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives.

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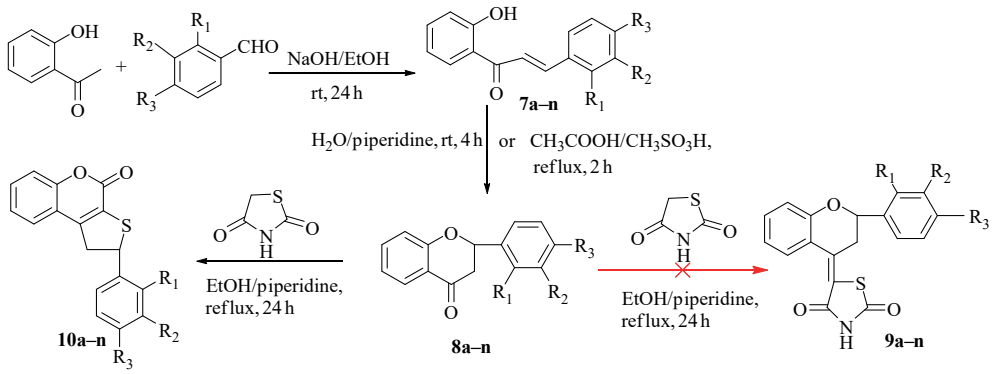
in the obtained compound. Furthermore, $^{13}C$ NMR spectra also confirmed that the obtained product had one less carbon atom signal. On the other hand, peaks of its IR spectrum appeared at 1716 $cm^{-1}$ and 1640 $cm^{-1}$, which showed there might be an unsaturated lactone moiety. The single crystal X-ray diffraction verified our speculation and the obtained compound was 2-(3-chlorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one (**10a**), which was not our desired compound **9a**.

In order to clarify the reaction mechanism, considering that the cyclisation of **7** to **8** in base or acid conditions is possibly a reversible reaction, we thought that compound **10** was obtained through the reaction of **7** and ethyl mercaptoacetate. A probable process for the formation of the product **10** is depicted in Scheme 2. Compound **8** and thiazolidine-2,4-dione are decomposed into **7** and ethyl mercaptoacetate, respectively, then Michael addition reaction is conducted between compound **7** and ethyl thioglycolate to produce an adduct**,** which by further reaction produced ethyl 3-(2-hydroxyphenyl)-5-phenyl-4,5-dihydrothiophene-2-carboxylate by Knoevenagel condensation. Finally the coumarin derivative **10** is obtained through intramolecular esterification.

A wide variety of 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives **10b–n** were also prepared using different substituted flavanones **8** under the same experimental conditions, as shown in Scheme 1. Among these substituted flavanones, compounds **8a**, **8b**, **8h**, **8l**, and **8m** were synthesised with high yields following the literature procedure.[20] The remaining compounds were prepared according to the reported procedure,[21] and reaction intermediates were directly used in the next reaction without further purification.

In order to further prove our analysis, the coumarin derivatives **10a–n** were also prepared through the reaction of compounds **7a–n** directly with thiazolidine-2,4-dione in ethanol in the presence of piperidine, as shown in Scheme 3. The yields of compounds **10a–n** through the two different synthetic routes in Scheme 1 and 3 were fairly similar.

Manna *et al.*[17] have also reported that dihydrothienocoumarins can be obtained through the condensation reaction of ethyl thioglycolate in the presence of piperidine in benzene, as shown in Scheme 4, which agreed with our speculation. Moreover, the IR and NMR properties of 2-aryl-1,2-dihydro(4*H*)thieno[2,3-*c*]benzo[*e*]




**a:** $R_1$=$R_3$=H, $R_2$=Cl **b:** $R_1$=Cl, $R_2$=$R_3$=H **c:** $R_1$=H, $R_2$=$R_3$=Cl

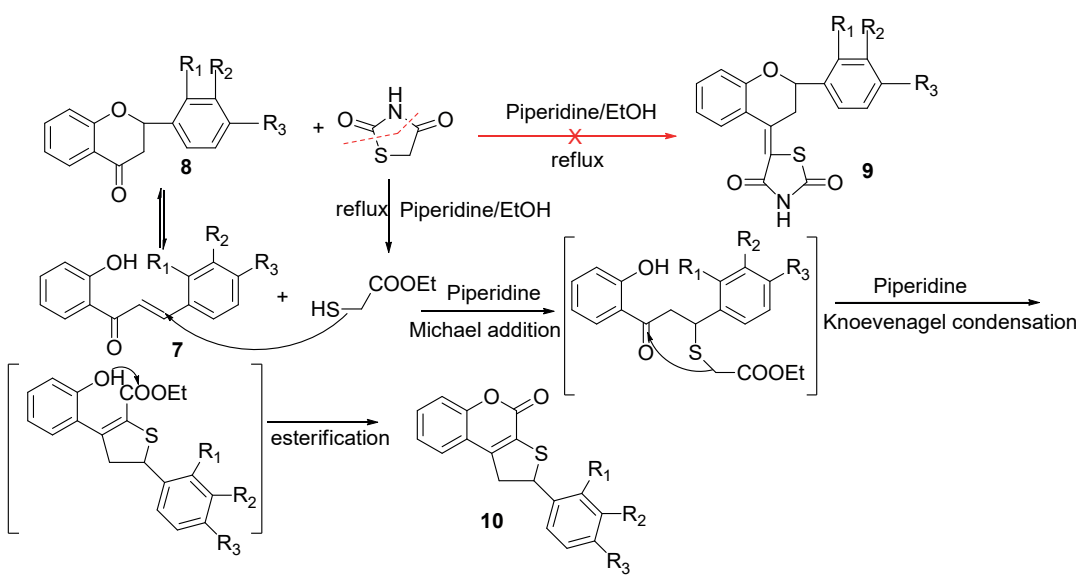
**d:** $R_1$=Br, $R_2$=$R_3$=H **e:** $R_1$=$R_2$=H, $R_3$=Br **f:** $R_1$=F, $R_2$=$R_3$=H

**g:** $R_1$=$R_3$=H, $R_2$=F **h:** $R_1$=$R_2$=$R_3$=H **i:** $R_1$=$CH_3$, $R_2$=$R_3$=H

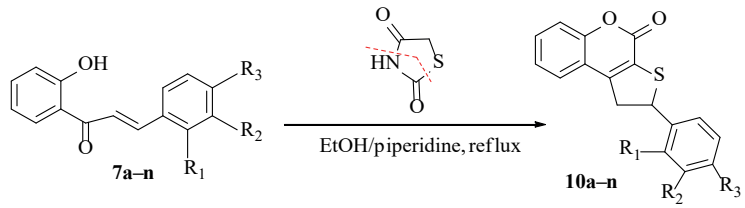
**j:** $R_1$=$R_3$=H, $R_2$=$CH_3$ **k:** $R_1$=$R_2$=H, $R_3$=$C(CH_3)_3$ **l:** $R_1$=$OCH_3$, $R_2$=$R_3$=H

**m:** $R_1$=$R_2$=H, $R_3$=$OCH_3$ **n:** $R_1$=H, $R_2$=$R_3$=$OCH_3$

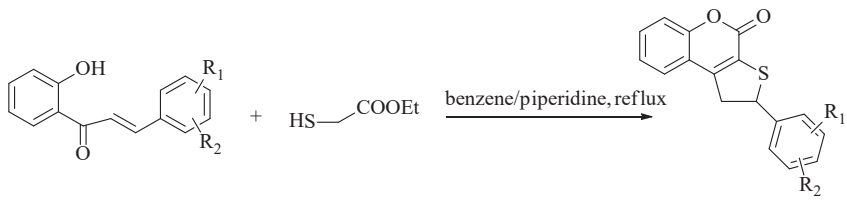
**Scheme 1** Synthetic route of compounds **10a–n**.




**Scheme 2** Proposed mechanism for the formation of compound **10**.




**Scheme 3** Intermediates **7** directly reacting with thiazolidine-2,4-dione to afford **10**.




**Scheme 4** Synthesis of dihydrothienocoumarins.

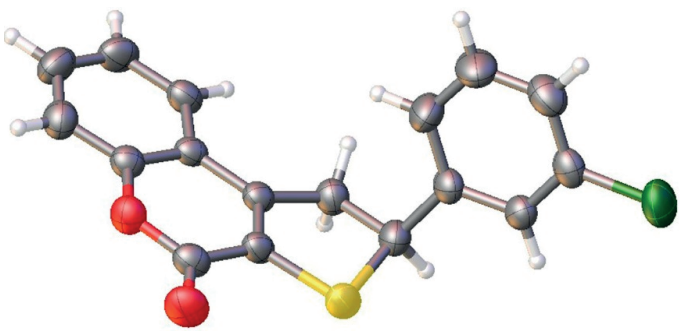


**Fig. 3** X-ray crystallographic structure of **10a**.

pyran-4-ones were studied by Robert *et al.*[22] and the crystal structure of 2-phenyldihydrothienocoumarin agrees with the results of the spectroscopic study; Robert *et al.*[18] have pointed out that X-ray diffraction and $^1$H NMR spectrometry could be used to illustrate the conformation of some kinds of dihydrothienocoumarins.

The structure of all the synthesised 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives **10a–n** have been firmly confirmed by means of the spectral analysis and elemental analysis. The structure of 2-(3-chlorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one (**10a**) has been further confirmed by its single crystal X-ray diffraction analysis as shown in Fig. 3. Most of these compounds are known except for compounds **10c**, **10f**, **10g**, **10k** and **10n**, but their melting points have not been reported in the publication. The crystal refinement data of **10a** are listed in Table 1.

### Invitro *antitumour evaluation*

The synthesised compounds **10a–n** were evaluated for their *in vitro* antitumour activities against five cancer cell lines. The results listed in Table 2 showed that most of the tested compounds had poor activity against these five cancer cell lines, except **10f** ($IC_{50}$ = 30–39 μM) and **10n** ($IC_{50}$ = 19–26 μM) which have moderate to good activities against A549, BGC-823, HCT116 and MDA-MB-453 cells. Especially, compound **10n** was found to exhibit similar activity against all tested types of cancer cells except for U87 as compared with the reference drug gefitinib. Comparing the activities of **10n** with those of **10m** and **10l**, it may be concluded that compounds carrying more $OCH_3$ groups in the phenyl ring are more active. All compounds **10a–n** displayed poor activity towards the cancer cell U87. It is worth noting that **10n** ($IC_{50}$ = 19.72 μM) showed a better performance against MDA-MB-453 cell line than gefitinib ($IC_{50}$ = 31.5 μM).

**Table 1** Crystal data and structure refinement information for the compound **10a**

| Formula | $C_{17}H_{11}ClO_2S$ |
|---|---|
| Formula weight/g | 314.02 |
| Temperature | 293.15 K |
| $\rho_{calc}$ g/cm$^3$ | 1.495 |
| Crystal system, space group | Monoclinic, $P2_1/c$ |
| Unit cell dimensions | $a$ = 14.8803 (10) Å, α = 90°<br>$b$ = 9.1115(5) Å, β = 110.750(8)°<br>$c$ = 11.0319(9) Å, γ = 90° |
| Volume | 1398.70(18) Å$^3$ |
| Z | 4 |
| M | 0.422 mm$^{-1}$ |
| F(000) | 648.0 |
| Crystal size | 0.4 × 0.3 × 0.3 mm |
| Theta range for data collection | 5.966 to 52.736° |
| Limiting indices | $-17 \le h \le 18$, $-9 \le k \le 11$, $-13 \le l \le 13$ |
| Reflections collected | 5920 |
| Independent reflections | 2845 [$R_{int}$ = 0.0218, $R_{sigma}$ = 0.0375] |
| Radiation | MoKα(λ = 0.71073) |
| Goodness-of-fit on F$^2$ | 1.051 |
| Data/restraints/parameters | 2845/0/190 |
| Largest diff. peak/hole / e | 0.42/−0.26e Å$^{-3}$ |
| Final R indices (I >2sigma(I)) | $R_1$ = 0.0439, $wR_2$ = 0.1006 |
| R indices (all data) | $R_1$ = 0.0597, $wR_2$ = 0.1096 |

## Experimental

Hydroxychalcones **7a–n** were prepared according to the literature procedure,[23] and recrystallised from EtOH. All the starting materials and solvents were purchased from common commercial suppliers and were used without purification. Melting points were recorded using a A XRC-1 micro melting point apparatus and are uncorrected. $^1$H NMR and $^{13}$C NMR were recorded with a Varian INOVA Gemini 400 spectrometer. Chemical shifts were reported in parts per million (δ) using TMS as internal standard and coupling constants were expressed in Hz. IR (KBr) spectra were recorded on a VECTOR22 and the values are expressed as $\nu_{max}$ cm$^{-1}$. The HRMS spectra were determined with a Bruker Amazon SL. Cancer cell lines were bought from Ji-Mian Bio-Tech. Ltd, Shanghai, P.R. China. Monitoring the reactions and checking the purity of the final products were carried out by TLC using precoated silica gel on aluminum sheets (60 mesh containing fluorescent indicator F254,

**Table 2** *In vitro* anticancer activities of synthesised compounds through the MTT assay

| Compound no. | $IC_{50}$ [a,b]/μM | | | | |
|---|---|---|---|---|---|
| | A549 | BGC-823 | HCT116 | MDA-MB-453 | U87 |
| **10a** | >80 | >80 | 64.65 | >80 | >80 |
| **10b** | >80 | >80 | 53.66 | >80 | >80 |
| **10c** | 55.18 | 61.51 | 63.19 | >80 | >80 |
| **10d** | 50.32 | 54.2 | 52.71 | >80 | >80 |
| **10e** | >80 | 64.76 | >80 | >80 | >80 |
| **10f** | 39.06 | 38.87 | 30.85 | 34.25 | >80 |
| **10g** | 46.35 | 52.83 | 65.88 | >80 | >80 |
| **10h** | >80 | 67.26 | >80 | >80 | >80 |
| **10i** | 62.37 | 76.44 | >80 | >80 | >80 |
| **10j** | >80 | >80 | 52.9 | >80 | >80 |
| **10k** | 35.53 | 44.23 | 65.42 | 47.35 | >80 |
| **10l** | 53.18 | 47.48 | 54.35 | 49.67 | >80 |
| **10m** | >80 | 47.14 | 56.42 | 38.06 | >80 |
| **10n** | 23.18 | 26.52 | 21.71 | 19.72 | >80 |
| TN[c] | 12.35 | 18.43 | 18.35 | 31.5 | 34.7 |

[a]The $IC_{50}$ values represent the concentration that causes 50% growth inhibition.
[b]The $IC_{50}$ values were the mean values of three repeated experiments within 5%.
[c]TN is gefitinib.

Merck) and visualisation of the spots was carried out under ultraviolet light at 365 and 254 nm.

*Synthesis of substituted flavanones (***8a**, **8b**, **8h**, **8l**, **8m***); general procedure*

These five compounds were synthesised according to the reported procedures.[20] A suspension of powdered **7** (5 mmol) in water (30 mL) containing a catalytic amount of piperidine was stirred for 4 h at room temperature. The formed solid was filtered off, washed with water, dried *in vacuo*, and recrystallised from EtOH to give pure flavanone **7** as needles in high yields. It may be pointed out here that our attempts to synthesise compounds **8c–g**, **8i–k** and **8n** in this way were unsuccessful.

*2-(3-Chlorophenyl)-2,3-dihydrochromen-4-one* (**8a**)

Pale-yellow solid, yield 93.6%; m.p. 97–99 °C (lit.[24] 98–99 °C); IR (KBr), $\nu_{max}$ $cm^{-1}$: 3058 (Ar=C–H), 2902 ($CH_2$), 1687 (C=O), 1466 (Ar, C=C), 1240 (Ar–O–CH). $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.81 (dd, 1H, *J* = 7.8, 1.4 Hz, ArH), 7.58–7.67 (m, 2H, ArH), 7.41–7.56 (m, 3H, ArH), 5.71 (dd, 1H, *J* = 13.0, 2.8 Hz, CH), 3.28 (dd, 1H, *J* = 16.8, 13.0 Hz, $CH_2$), 2.87 (dd, 1H, *J* = 16.8, 2.9 Hz, $CH_2$).

*2-(2-Chlorophenyl)-2,3-dihydrochromen-4-one* (**8b**)

Pale-yellow solid, yield 97.6%; m.p. 90–92 °C (lit.[25] 96–97 °C); IR (KBr), $\nu_{max}$ $cm^{-1}$: 3053 (Ar=C–H), 2916 ($CH_2$), 1694 (C=O), 1464 (C=C), 1242 (Ar–O–CH). $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.87–7.75(m, 2H, ArH), 7.66–7.59 (m, 1H, ArH), 7.55 (dd, *J* = 7.6, 1.6 Hz, 1H, ArH), 7.51–7.41 (m, 2H, ArH), 7.15 (dd, *J* = 8.4, 1.2 Hz, 2H, ArH), 5.92 (dd, *J* = 13.6, 2.8 Hz, 1H, CH), 3.28 (dd, *J* = 16.8, 13.6 Hz, 1H, $CH_2$), 2.84 (dd, *J* = 16.8, 2.8 Hz, 1H, $CH_2$).

*2-Phenyl-2,3-dihydrochromen-4-one* (**8h**)

Pale-yellow solid, yield 96.4%; m.p. 75–77 °C (lit.[24] 75–76 °C); IR (KBr), $\nu_{max}$ $cm^{-1}$: 3051 (Ar=C–H), 2930 ($CH_2$), 2913 ($CH_2$), 1691 (C=O), 1464 (Ar, C=C), 1252 (Ar–O–CH). $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.94 (dd, 1H, *J* = 8.1, 1.5 Hz, ArH), 7.37–7.54 (m, 6H, ArH), 7.05–7.08 (m, 2H, ArH), 5.49 (dd, 1H, *J* = 13.3, 2.6 Hz, CH), 3.10 (dd, 1H, *J* = 16.9, 13.4 Hz, $CH_2$), 2.90 (dd, 1H, *J* = 16.9, 2.8 Hz, $CH_2$).

*2-(2-Methoxyphenyl)-2,3-dihydrochromen-4-one* (**8l**)

Pale-yellow solid, yield 92.8%; m.p. 112–113 °C (lit.[26] 113–114 °C); IR (KBr), $\nu_{max}$ $cm^{-1}$: 3058 (Ar=C–H), 2911 ($CH_2$), 1694 (C=O), 1461 (Ar, C=C), 1244 (Ar–O–CH).$^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.84 (dd, *J* = 7.9, 1.4 Hz, 1H, Ar), 7.53 (dd, *J* = 7.6, 1.2 Hz, 1H, Ar), 7.39–7.28 (m, 2H, ArH), 7.09–6.96 (m, 4H, Ar), 5.34 (dd, *J* = 12.1, 2.9 Hz, 1H, CH), 3.83 (s, 3H, $OCH_3$), 3.40 (dd, 1H, *J* = 17.0, 13.0 Hz, $CH_2$), 2.56 (dd, 1H, *J* = 17.0, 2.1 Hz, $CH_2$).

*2-(4-Methoxyphenyl)-2,3-dihydrochromen-4-one* (**8m**)

Pale-yellow solid, yield 86.3%; m.p. 86–88 °C (lit.[27] 87–88 °C); IR (KBr), $\nu_{max}$ $cm^{-1}$: 3056 (Ar=C–H), 2915 ($CH_2$), 1690 (C=O), 1457 (Ar, C=C), 1247 (Ar–O–CH). $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.80 (dd, *J* = 8.0, 1.4 Hz, 1H, Ar), 7.59 (td, *J* = 7.9, 1.3 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.09 (t, *J* = 7.7 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H, Ar), 5.60 (dd, *J* = 13.0, 2.8 Hz, 1H, CH), 3.77 (s, 3H, $OCH_3$), 3.28 (dd, *J* = 16.7, 13.0 Hz, 1H, $CH_2$), 2.78 (dd, *J* = 16.8, 2.9 Hz, 1H, $CH_2$).

*Synthesis of 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives* (**10a**, **10b**, **10h**, **10l**, **10m**)*; general procedure*

A mixture of compound **8** (2 mmol) and thiazolidine-2,4-dione (0.28 g, 2.4 mmol) in ethanol (20 mL) in the presence of piperidine (0.4 mL) was refluxed for 20 h. On cooling the reaction mixture to room temperature with stirring, the white crude product was precipitated, filtered, washed with ethanol, and dried, and recystallised from methanol to obtain pure product **8** with about 40% yield.

*2-(3-Chlorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10a**)

CAS No.: 73386-35-3; white solid, yield 46.3%; m.p. 166–168 °C; IR (KBr), $\nu_{max}$ $cm^{-1}$: 3010 (Ar=C–H), 1716 (C=O), 1640 (C=C), 1547 (Ar). $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.64 (d, *J* = 7.8 Hz, 1H, ArH), 7.61–7.53 (m, 2H, ArH), 7.53–7.43 (m, 2H, ArH), 7.43–7.34 (m, 3H, ArH), 5.42 (dd, *J* = 9.6, 7.1 Hz, 1H, CH), 4.07 (dd, *J* = 18.2, 9.6 Hz, 1H, $CH_2$), 3.80 (dd, *J* = 18.2, 7.1 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.5 (C=O), 153.1 (ArH), 156.5 (C=O), 153.1 (ArH), 147.4 (C=C–S), 144.9 (ArH), 133.7 (ArH), 131.2 (ArH), 131.1 (ArH), 128.3 (ArH), 127.7 (ArH), 126.6 (ArH), 126.4 (ArH), 125.7 (ArH), 125.3 (ArH), 118.3 (C=C–S), 116.9 (ArH), 50.8 ($CH_2$), 43.1 (CH); MS (ESI) *m/z*, $[M + H]^+$ calcd 315.02; found: 314.89; Anal. calcd for $C_{17}H_{11}ClO_2S$: C, 64.86; H, 3.52; S, 10.19; found: C, 64.63; H, 3.49; S, 10.17%.

*2-(2-Chlorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10b**)

CAS No.: 73386-34-2; white solid, yield 49.1%; m.p. 163–165 °C; IR (KBr), $\nu_{max}$ $cm^{-1}$: 3075 (Ar=C–H), 1712 (C=O), 1640 (C=C), 1543 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.73 (d, *J* = 7.7 Hz, 1H, ArH), 7.60 (t, *J* = 7.7 Hz, 1H, ArH), 7.56–7.46 (m, 3H, ArH), 7.41 (t, *J* = 7.5 Hz, 1H, ArH), 7.38–7.30 (m, 2H, ArH), 5.59 (dd, *J* = 9.3, 5.2 Hz, 1H, CH), 4.05 (dd, *J* = 18.2, 9.5 Hz, 1H, $CH_2$), 3.93 (dd, *J* = 18.2, 5.0 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$,100 MHz): δ 156.6 (C=O), 153.1 (ArH), 147.7 (C=C–S), 139.4 (ArH), 132.7 (ArH), 131.2 (ArH), 130.1 (ArH), 130.1 (ArH), 128.4 (ArH), 128.3 (ArH), 126.2 (ArH), 125.8 (ArH), 125.4 (ArH), 118.3 (C=C–S), 116.9 (ArH), 48.1 ($CH_2$), 40.9 (CH); HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 337.0066; found: 337.0069; Anal. calcd for $C_{17}H_{11}ClO_2S$: C, 64.86; H, 3.52; S, 10.19; found: C, 64.74; H, 3.62; S, 10.16%.

*2-Phenyl-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10h**)

CAS No.: 73386-25-1; white solid, yield 45.7%; m.p. 142–143 °C; IR (KBr), $\nu_{max}$ $cm^{-1}$: 3086 (Ar=C–H), 1709 (C=O), 1632 (C=C), 1547 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.66 (d, *J* = 7.7 Hz, 1H, ArH), 7.58 (t, *J* = 7.7 Hz, 1H, ArH), 7.49 (d, *J* = 7.2 Hz, 3H, ArH), 7.42–7.29 (m, 4H, ArH), 5.41 (t, *J* = 8.5 Hz, 1H, CH), 4.06 (dd, *J* = 18.0, 9.4 Hz, 1H, $CH_2$), 3.78 (dd, *J* = 18.0, 7.5 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.5 (C=O), 153.0 (ArH), 147.6 (C=C–S), 142.2 (ArH), 131.0 (ArH), 129.3 (ArH), 128.4 (ArH), 127.6 (ArH), 126.8 (ArH), 125.7 (ArH), 125.4 (ArH), 118.3 (C=C–S), 116.9 (ArH), 51.8 ($CH_2$), 43.2 (CH). HRMS (ESI) *m/z*, $[M + Na]^+$, calcd 303.0456; found: 303.0456; Anal. calcd for $C_{17}H_{12}O_2S$: C, 72.83; H, 4.31; S, 11.44; found: C, 72.56; H, 4.46; S, 11.46%.

*2-(2-Methoxyphenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10l**)

CAS No.: 73386-29-5; white solid, yield 46.1%; m.p. 122–124 °C; IR (KBr), $\nu_{max}$ $cm^{-1}$: 3057 (Ar=C–H), 1715 (C=O), 1638 (C=C), 1546 (Ar), 1240 (Ar–O–$CH_3$); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.72 (dd,

*J* = 7.8, 1.2 Hz, 1H, ArH), 7.61–7.55 (m, 1H, ArH), 7.47 (d, *J* = 7.7 Hz, 1H, ArH), 7.43–7.37 (m, 1H, ArH), 7.35–7.27 (m, 2H, ArH), 7.06 (d, *J* = 8.1 Hz, 1H, ArH), 6.92 (t, *J* = 7.5 Hz, 1H, ArH), 5.48 (dd, *J* = 9.1, 6.2 Hz, 1H, CH), 3.97–3.85 (m, 2H, $CH_2$), 3.84 (s, 3H, $OCH_3$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.7 (C=O), 152.9 (ArH), 152.6 (ArH), 147.7 (C=C–S), 130.9 (ArH), 129.7 (ArH), 129.6 (ArH), 127.0 (ArH), 126.8 (ArH), 125.6 (ArH), 125.4 (ArH), 121.1 (ArH), 118.4 (C=C–S), 116.8 (ArH), 111.7 (ArH), 56.2 ($OCH_3$), 45.6 ($CH_2$), 39.4 (CH); HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 333.0561; found: 333.0562; Anal. calcd for $C_{18}H_{14}O_3S$: C, 69.66; H, 4.55; S, 10.33; found: C, 69.76; H, 4.41; S, 10.43%.

*2-(4-Methoxyphenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10m**)

CAS No.: 73386-31-9; white solid, yield 44.3%; m.p. 136–137 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3012 (Ar=C–H), 1718 (C=O), 1643 (C=C), 1541 (Ar), 1247 (Ar–O–$CH_3$); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.65 (dd, *J* = 7.8, 1.2 Hz, 1H, ArH), 7.56 (dd, *J* = 7.2, 1.3 Hz, 1H, ArH), 7.47 (d, *J* = 8.3 Hz, 1H, ArH), 7.43–7.35 (m, 3H, ArH), 6.94–6.89 (m, 2H, ArH), 5.41 (t, *J* = 8.6 Hz, 1H, CH), 4.01 (dd, *J* = 18.0, 9.3 Hz, 1H, $CH_2$), 3.76 (s, 3H, $OCH_3$), 3.74 (dd, *J* = 18.4, 7.6 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 159.4 (C=O), 156.5 (ArH), 153.0 (ArH), 147.6 (C=C–S), 133.8 (ArH), 131.0 (ArH), 128.9 (ArH), 126.8 (ArH), 125.6 (ArH), 125.3 (ArH), 118.4 (C=C–S), 116.8 (ArH), 114.6 (ArH), 55.6 ($OCH_3$), 51.6 ($CH_2$), 43.3 (CH); Anal. calcd for $C_{18}H_{14}O_3S$: C, 69.66; H, 4.55; S, 10.33; found: C, 69.42; H, 4.73; S, 10.45%.

*Synthesis of substituted flavanones* (**8c–g, 8i–k, 8n**)*; general procedure*

These compounds were synthesised according to the literature procedures.[21] A suspension of compound **7** (10 mmol) in acetic acid (25 mL) and a catalytic amount of methanesulphonic acid (10 mol %) was refluxed for 2 h. The reaction solution was diluted with water (150 mL). The product was extracted with dichloromethane (20 mL × 3), dried over anhydrous sodium sulfate, and the solvent was evaporated *in vacuo* to give an oily liquid, which was the crude product. It was difficult to separate the products because of their similar Rf value between chalcones and products.

*Synthesis of 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives* (**10c–g, 10i–k, 10n**)*; general procedure*

The crude products **8** were directly reacted with thiazolidine-2,4-dione (1.4 g, 12 mmol) in ethanol (30 mL) in the presence of piperidine at 78 °C for 20 h. The white crude product was precipitated when the reaction mixture was cooled to room temperature with stirring. Then, it was filtered, washed with ethanol, dried, and recystallised from methanol to obtain pure products **10** with about 40% yields.

*2-(3,4-Dichlorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10c**)

White solid, yield 42.7%; m.p. 206–208 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3015 (Ar=C–H), 1721 (C=O), 1639 (C=C), 1540 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.78 (d, *J* = 2.1 Hz, 1H, ArH), 7.65–7.56 (m, 3H, ArH), 7.48 (dd, *J* = 8.4, 2.2 Hz, 2H, ArH), 7.39 (td, *J* = 7.7, 1.1 Hz, 1H, ArH), 5.42 (dd, *J* = 9.7, 6.7 Hz, 1H, CH), 4.07 (dd, *J* = 18.2, 9.7 Hz, 1H, $CH_2$), 3.81 (dd, *J* = 18.2, 6.7 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.5 (C=O), 153.1 (Ar–C), 147.3 (C=C–S), 143.7 (Ar–C), 131.7 (Ar–C), 131.5 (Ar–C), 131.1 (Ar–C), 130.9 (Ar–C), 130.0 (Ar–C), 128.0 (Ar–C), 126.4 (Ar–C), 125.4 (Ar–C), 118.3 (C=C-S), 116.9 (Ar–C), 50.0 ($CH_2$), 43.1 (CH); HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 370.9676; found: 370.9676; Anal. calcd for $C_{17}H_{10}Cl_2O_2S$: C, 58.47; H, 2.89; S, 9.18; found: C, 58.83; H, 3.12; S, 9.37%.

*2-(2-Bromophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10d**)

CAS No.: 145626-19-3; white solid, yield 49.3%; m.p. 165–167 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3062 (Ar =C–H), 1713 (C=O), 1645 (C=C), 1542 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.72 (m, 2H, ArH), 7.60 (m, 1H, ArH), 7.50 (m, 2H, ArH), 7.44–7.35 (m, 2H, ArH), 7.26 (td, *J* = 7.7, 1.6 Hz, 1H, ArH), 5.52 (dd, *J* = 9.4, 5.0 Hz, 1H, CH), 4.05 (dd, *J* = 18.3, 9.4 Hz, 1H, $CH_2$), 3.93 (dd, *J* = 18.2, 5.0 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.6 (C=O), 153.1 (Ar–C), 147.7 (C=C–S), 141.0 (Ar–C), 133.4 (Ar–C), 131.2 (Ar–C), 130.3 (Ar–C), 129.0 (Ar–C), 128.3 (Ar–C), 126.1 (Ar–C), 125.8 (Ar–C), 125.4 (Ar–C), 123.7 (Ar–C), 118.3 (C=C–S), 116.9 (Ar–C), 50.8 ($CH_2$), 41.0 (CH). HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 380.9561; found: 380.9554; Anal. calcd for $C_{17}H_{11}BrO_2S$: C, 56.84; H, 3.09; S, 8.93; found: C, 56.61; H, 2.89; S, 9.04%.

*2-(4-Bromophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10e**)

CAS No.: 145626-21-7; white solid, yield 52.8%; m.p. 181–182 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3067 (Ar=C–H), 1713 (C=O), 1645 (C=C), 1542 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.64 (dd, *J* = 7.8, 1.4 Hz, 1H, ArH), 7.61–7.53 (m, 3H, ArH), 7.46–7.37 (m, 4H, ArH), 5.39 (dd, *J* = 9.5, 6.6 Hz, 1H, CH), 4.06 (dd, *J* = 18.1, 9.6 Hz, 1H, $CH_2$), 3.76 (dd, *J* = 18.1, 6.9 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.5 (C=O), 153.1 (Ar–C), 147.4 (C=C–S), 141.9 (Ar–C), 132.2 (Ar–C), 131.1 (Ar–C), 130.0 (Ar–C), 126.6 (Ar–C), 125.7 (Ar–C), 125.4 (Ar–C), 121.4 (Ar–C), 118.3 (C=C–S), 116.8 (Ar–C), 50.8 ($CH_2$), 43.1 (CH); Anal. calcd for $C_{17}H_{11}BrO_2S$: C, 56.84; H, 3.09; S, 8.93; found: C, 56.43; H, 3.06, S, 9.17%.

*2-(2-Fluorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10f**)

White solid, yield 50.3%; m.p. 141–143 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3096 (Ar=C–H), 1715 (C=O), 1645 (C=C), 1547 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.69 (dd, *J* = 7.8, 1.1 Hz, 1H, ArH), 7.62–7.47 (m, 3H, ArH), 7.43–7.35 (m, 2H, ArH), 7.23 (dt, *J* = 10.1, 7.6 Hz, 2H, ArH), 5.55 (dd, *J* = 9.7, 6.2 Hz, 1H, CH), 4.06 (dd, *J* = 18.1, 9.7 Hz, 1H, $CH_2$), 3.86 (dd, *J* = 18.1, 6.2 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 160.1 (d, $J_{C-F}$ = 244.5 Hz, Ar–C), 156.5 (C=O), 153.0 (Ar–C), 147.6 (C=C–S), 131.1 (Ar–C), 130.5 (d, $J_{C-F}$ = 8.4 Hz, Ar–C), 129.1 (d, $J_{C-F}$ = 13.2 Hz, Ar–C), 129.0 (d, $J_{C-F}$ = 3.4 Hz, Ar–C), 126.3 (Ar–C), 125.7 (Ar–C), 125.4 (Ar–C), 118.3 (C=C–S), 116.9 (Ar–C), 116.2 (d, $J_{C-F}$ = 21.3 Hz, Ar–C), 44.6 (d, $J_{C-F}$ = 2.7 Hz, $CH_2$), 41.6 (CH). HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 321.0361; found: 321.0360; Anal. calcd for $C_{17}H_{11}FO_2S$: C, 68.44; H, 3.72; S, 10.75; found: C, 68.17; H, 3.84; S, 10.78%.

*2-(3-Fluorophenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10g**)

White solid, yield 48.7%; m.p. 146–148 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3094 (Ar=C–H), 1717 (C=O), 1641 (C=C), 1549 (Ar); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.65 (dd, *J* = 7.8, 1.4 Hz, 1H, ArH), 7.61–7.5 (m, 1H, ArH), 7.48 (dd, *J* = 8.3, 0.7 Hz, 1H, ArH), 7.44–7.31 (m, 4H, ArH), 7.18–7.12 (m, 1H, ArH), 5.42 (dd, *J* = 9.5, 7.2 Hz, 1H, CH), 4.07 (dd, *J* = 18.1, 9.5 Hz, 1H, $CH_2$), 3.80 (dd, *J* = 18.1, 7.2 Hz, 1H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 162.7 (d, $J_{C-F}$ = 242.5 Hz, Ar–C), 156.5 (C=O), 153.1 (Ar–C), 147.5 (C=C–S), 145.2 (d, $J_{C-F}$ = 7.3 Hz, Ar–C), 131.3 (d, $J_{C-F}$ = 8.4 Hz, Ar–C), 131.1 (Ar–C), 126.6 (Ar–C), 125.7 (Ar–C), 125.3 (Ar–C), 123.8 (d, $J_{C-F}$ = 2.7 Hz, Ar–C), 118.3 (C=C–S), 116.9 (Ar–C), 115.2 (d, $J_{C-F}$ = 20.9 Hz, Ar–C), 114.6 (d, Ar–C, $J_{C-F}$ = 21.9 Hz), 50.9 ($CH_2$), 43.3 (CH). Anal. calcd for $C_{17}H_{11}FO_2S$: C, 68.44; H, 3.72; S, 10.75; found: C, 68.23; H, 3.92; S, 10.41%.

*2-(*o*-Tolyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10i**)

CAS No.: 73386-26-2; white solid, yield 43.8%; m.p. 151–152 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3071 (Ar=C–H), 1711 (C=O), 1646 (C=C), 1547 (Ar), 1376 ($CH_3$); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.70 (d, *J* = 7.6 Hz, 1H, ArH), 7.59 (t, *J* = 7.8 Hz, 1H, ArH), 7.47 (dd, *J* = 11.8, 5.5 Hz, 2H, ArH), 7.40 (t, *J* = 7.5 Hz, 1H, ArH), 7.25–7.16 (m, 3H, ArH), 5.55 (dd, *J* = 9.1, 6.9 Hz, 1H, CH), 4.01 (dd, *J* = 18.0, 9.4 Hz, 1H, $CH_2$), 3.81 (dd, *J* = 18.0, 6.7 Hz, 1H, $CH_2$), 2.39 (s, 3H, $CH_3$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.6 (C=O), 153.0 (Ar–C), 147.9 (C=C–S), 139.8 (Ar–C), 135.9 (Ar–C), 131.0 (Ar–C), 130.9 (Ar–C), 128.2 (Ar–C), 127.0 (Ar–C), 126.6 (Ar–C), 125.7 (Ar–C), 125.4 (Ar–C), 125.4 (Ar–C), 118.3 (C=C-S), 116.9 (Ar–C), 48.4 (CH2), 41.8 (CH), 19.7 ($CH_3$); HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 317.0612; found: 317.0613; Anal. calcd for $C_{18}H_{14}O_2S$: C, 73.44; H, 4.79; S, 10.89; found: C, 73.56; H, 4.62; S, 10.81%.

*2-(*m*-Tolyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10j**)

CAS No.: 73386-27-3; white solid, yield 44.5%; m.p. 153–154 °C; IR (KBr), $\nu_{max}$ cm$^{-1}$: 3057 (Ar=C–H), 1710 (C=O), 1640 (C=C), 1542 (Ar), 1373 ($CH_3$); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.64 (dd, *J* = 7.8, 1.3 Hz, 1H, ArH), 7.58 (m, 1H, ArH), 7.47 (dd, *J* = 8.3, 0.8 Hz, 1H, ArH), 7.39 (td, *J* = 7.8, 1.1 Hz, 1H, ArH), 7.33–7.22 (m, 3H, ArH), 7.15–7.10 (m, 1H, ArH), 5.37 (dd, *J* = 9.4, 8.1 Hz, 1H, CH), 4.04 (dd, *J* = 18.1, 9.5 Hz, 1H, $CH_2$), 3.75 (dd, *J* = 18.1, 8.0 Hz, 1H, $CH_2$), 2.30 (s, 3H, $CH_3$); $^{13}$C NMR

(DMSO-$d_6$, 100 MHz): δ 156.5 (C=O), 153.0 (Ar–C), 147.6 (C=C–S), 141.9 (Ar–C), 138.5 (Ar–C), 131.0 (Ar–C), 129.2 (Ar–C), 129.0 (Ar–C), 128.3 (Ar–C), 126.8 (Ar–C), 125.6 (Ar–C), 125.4 (Ar–C), 124.7 (Ar–C), 118.3 (C=C–S), 116.8 (Ar–C), 51.8 ($CH_2$), 43.3 (CH), 21.5 ($CH_3$); Anal. calcd for $C_{18}H_{14}O_2S$: C, 73.44; H, 4.79; S, 10.89; found: C, 73.35; H, 4.72; S, 10.90%.

*2-(4-(tert-Butyl)phenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10k**)

White solid, yield 42.9%; m.p. 171–172 °C; IR (KBr), $\nu_{max}$ $cm^{-1}$: 3092 (Ar=C–H), 1709 (C=O), 1638 (C=C), 1542 (Ar), 1381 (*tert*-butyl); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.64 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.60–7.55 (m, 1H), 7.47 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.42–7.36 (m, 5H), 5.37 (dd, *J* = 9.2, 7.7 Hz, 1H), 4.02 (dd, *J* = 18.0, 9.3 Hz, 1H), 3.76 (dd, *J* = 18.0, 7.7 Hz, 1H), 1.26 (s, 9H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) δ: 156.6 (C=O), 153.0 (Ar–C), 150.9 (Ar–C), 147.9 (C=C–S), 139.0 (Ar–C), 131.0 (Ar–C), 127.3 (Ar–C), 126.8 (Ar–C), 126.0 (Ar–C), 125.6 (Ar–C), 125.3 (Ar–C), 118.3 (C=C–S), 116.8 (Ar–C), 51.6 ($CH_2$), 43.2 (CH), 34.7 ($C(CH_3)_3$), 31.5 ($C(CH_3)_3$); HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 359.1082; found: 359.1083; Anal. calcd for $C_{21}H_{20}O_2S$: C, 74.97; H, 5.99; S, 9.53; found: C, 74.64; H, 6.18; S, 9.72%.

*2-(3,4-Dimethoxyphenyl)-1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one* (**10n**)

White solid, yield 40.6%; m.p. 144–146 °C; IR (KBr), $\nu_{max}$ $cm^{-1}$: 3012 (Ar=C–H), 1714 (C=O), 1636 (C=C), 1540 (Ar), 1241 (Ar–O–$CH_3$); $^1$H NMR (DMSO-$d_6$, 400 MHz): δ 7.65 (d, *J* = 7.7 Hz, 1H, ArH), 7.58 (t, *J* = 7.7 Hz, 1H, ArH), 7.48 (d, *J* = 8.2 Hz, 1H, ArH), 7.39 (t, *J* = 7.5 Hz, 1H, ArH), 7.14 (s, 1H, ArH), 6.96 (dd, *J* = 16.3, 8.3 Hz, 2H, ArH), 5.40 (t, *J* = 9.0 Hz, 1H, CH), 4.01 (dd, *J* = 18.0, 9.3 Hz, 1H, $CH_2$), 3.80 (dd, *J* = 18.0, 6.2 Hz, 1H, $CH_2$), 3.75 (s, 3H, $OCH_3$), 3.74 (s, 3H, $OCH_3$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): δ 156.6 (C=O), 153.0 (Ar–C), 149.3 (Ar–C), 149.0 (Ar–C), 147.7 (C=C–S), 133.7 (Ar–C), 131.0 (Ar–C), 126.8 (Ar–C), 125.6 (Ar–C), 119.9 (Ar–C), 118.4 (C=C–S), 116.8 (Ar–C), 112.3 (Ar–C), 111.7 (Ar–C), 56.0 ($OCH_3$), 52.3 ($CH_2$), 43.3 (CH); HRMS (ESI) *m/z*, $[M + Na]^+$ calcd 363.0667; found: 363.0665; Anal. calcd for $C_{19}H_{16}O_4S$: C, 67.04; H: 4.74; S: 9.42; found: C, 66.85; H, 4.85; S, 9.46%.

*Crystal structure of* **10a**

A saturated solution of compound **10a** in $CH_2Cl_2$ at room temperature enabled slow solvent evaporation to improve crystal growth. A suitable crystal was selected and placed on a Xcalibur Eos diffractometer. The crystal was kept at 293.15 K during data collection. Using Olex2,[28] the structure was resolved with a ShelXS structure solution programme using direct methods and refined with a ShelXL refinement package using least squares minimisation (crystal information is shown in Table 1).[29]

In vitro *antitumour evaluation; general procedure*

All the synthesised compounds (**10a–n**) were screened for their *in vitro* antitumour activity against human lung cancer cell line (A549), gastric cancer cell line (BGC-823), colon cancer cell line (HCT116), breast cancer cell line (MDA-MB-453), and glioma cell line (U87) by the MTT assay. Briefly, cells ($3 \times 10^4$ $mL^{-1}$) were seeded in 96-well plates and cultured for 24 h, followed by various concentration of compounds from 50 μM to 1.56 μM treatment for 48 h at 37 °C, 5% $CO_2$. Then, 20 μL of 5 mg $mL^{-1}$ MTT was added per well and incubated for another 4 h at 37 °C, the supernatant fluid was removed, and DMSO was added 150 μL/well for 15–20 min. The light absorptions (OD) were measured at 570 nm with a SpectraMAX M5 microplate spectrophotometer (Molecular Devices). Gefitinib (TN) was used as the reference drug for antitumour evaluation, with the tested compounds assessed under similar conditions for comparison. The response parameter calculated was the $IC_{50}$ value, which corresponds to the concentration required for 50% inhibition of cell viability. The data for the antibacterial activity are presented in Table 3.

## Conclusion

In summary, a series of 1*H*-thieno[2,3-*c*]chromen-4(2*H*)-one derivatives were synthesised through Knoevenagel condensation reactions in the presence of piperidine in ethanol. A new process for the formation of coumarin derivatives was discovered, and the reaction mechanism was clarified. All the synthesised compounds were characterised by IR, $^1$H NMR, $^{13}$C NMR, HRMS, and by elemental analysis. The structure of **10a** has been confirmed by a single crystal X-ray diffraction analysis. Bioassay results indicated that most of the tested compounds have poor activity against these five cancer cell lines except for **10f** and **10n**, which have moderate to good activities against A549, BGC-823, HCT116 and MDA-MB-45 cell lines. Especially, compound **10n** which was found to exhibit similar activity against all tested types of cancer cells except for U87 as compared to the reference drug, gefitinib (TN).

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## Electronic Supplementary Information

NMR spectra and HRMS spectra are available from: stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data

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