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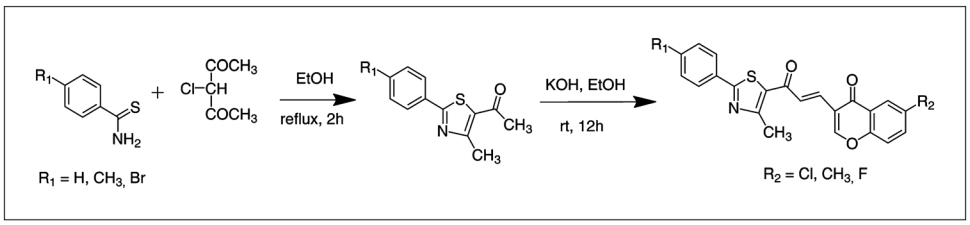

2-Aryl-4-methyl-5-acetylthiazoles, which were prepared from arylthioamides and chloroacetylacetone, were treated with 6-substituted-3-formylchromones or arylaldehydes to give a series of eighteen new thiazolylchalcones in good yields. The structures of all the synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, and ES-MS spectrometry. Additionally, the crystal structures of two of these chalcones were determined by X-ray diffraction analysis.

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INTRODUCTION

The treatment of infectious diseases remains an important issue because of a combination of factors including emerging infectious diseases and the increasing number of multidrug resistant microbial pathogens. This problem is particularly pronounced for the Gram-positive bacteria [1]. The therapeutic problem is increasingly important part of hospitalized patients, immunosuppressed patients with AIDS, and those undergoing anticancer therapy or organ transplants. Despite a large number of antibiotics and chemotherapeutics available for medical use, the emerging resistance to old and new antibiotics has created a substantial need for new classes of antibacterial agents. A potential approach to overcome antibiotic resistance in bacteria is to design innovative agents with a different mode of action so that no cross resistance with present drugs can occur [2].

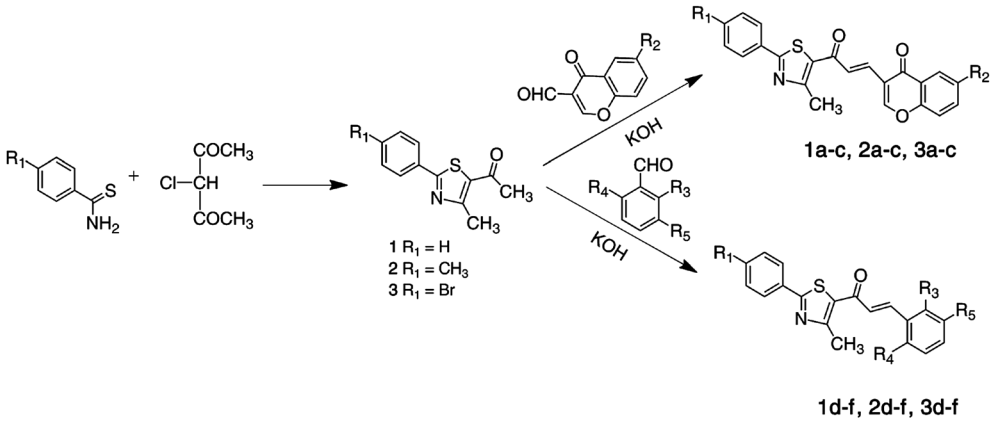
Thiazoles, chromones, and their derivatives have attracted interest over the years because of their varied biological activities [3]. Substituted chromones of both synthetic and natural origin also exhibit a broad spectrum of biological activities such as antibacterial [4], antiviral [5], and antifungal [6] activities. On the other hand, chalcones, a biosynthetic product of the shikimate pathway, is a separate class of structures, which have a wide range of biological properties. Chalcones are precursors of various flavones and key intermediates for the combinatorial assembly of different heterocyclic scaffolds. Chalcones (1,3-diaryl propenone or 1,3-diphenyl-2-propen-1-one) constitute an important group of natural products, some of which possess a wide range of biological effects, such as antibacterial [7], antitumor [8], antioxidant [9], antifungal [10], antiviral [11], and anti-inflammatory [12] activities and also act as tyrosinase inhibitors [13] and insect anti-feedent [14].

In view of the above-mentioned findings, and as a continuation of our effort to identify new candidates that may be value in designing new, potent, selective, and less toxic bioactive agents [15], we report, the synthesis and characterization of a series of new chalcones containing thiazoles. To obtain the new compounds with both thiazole and chromone nucleus in the same molecule, we synthesised a series of chalcones using the condensation of 2-aryl-4-methyl-5-acetylthiazoles with various substituted 3-formylchromones. To help elucidate the structure-activity relationships, and the importance of the pharmacophore chromone nucleus, we also synthesized the simplified analogs obtained by eliminating the chromone nucleus and replacing it with substituted phenyl rings.

RESULTS AND DISCUSSION

The Claisen-Schmidt condensation was used for the synthesis of 18 chalcones derivatives [16]. The starting 2-aryl-4-methyl-5-acetylthiazoles (**1–3**) were prepared

Scheme 1. Synthesis of 2-aryl-4-methyl-5-acetylthiazoles **1–3** and chalcones **1a–f**, **2a–f**, and **3a–f**.



by the condensation (Hantzsch reaction) of some arylthioamides (thiobenzamide, 4-methylthiobenzamide, and 4-bromothiobenzamide) with 3-chloroacetylacetone in ethanol under reflux, with a good yields (Scheme 1) with key spectroscopic data identical to literature values [17]. The reaction of the 2-aryl-4-methyl-5-acetylthiazole (**1–3**) separately with different chromones and available aldehydes in the presence of catalytic amount of solid KOH in ethanol resulted in the title compounds (**1a–f**, **2a–f**, and **3a–f**) in high yields (Scheme 1, Table 1). The structures of these compounds were established on the basis of their spectroscopic and diffraction data.

The IR spectra of the compounds, in general, exhibited the absorption band of conjugated carbonyl group at about 1670–1656 cm^{-1} and characteristic C=C band at 1592–1603 cm^{-1}. The ES-MS of the compounds showed $[M+H]^+$ or peaks corresponding to their molecular formulae. The NMR spectra (^1H and ^{13}C) are consistent with the proposed structures. Chalcones **1a–c**, **2a–c**, and **3a–c** in their ^1H NMR showed a singlet at δ 8.14 for H-2, a doublet doublet at δ 7.65 (J = 2 and 8 Hz) for H-7, a doublet at δ 7.40 (J = 8 Hz) for H-8, and a doublet at δ 7.80 ppm (J = 2 Hz) for H-5 of the chromones moiety. All the other aromatic protons were observed at δ 7.50–6.92. The protons of the methyl group of thiazole moiety appeared as a singlet at δ 2.87. In the ^{13}C NMR spectrum, the two carbonyl carbons appeared at δ 182.98–183.22 (C-1) and δ 175.07–176.35 (C-4). The olefinic carbons were visible at δ 141.50–135.00 and δ 126.30–129.61. The methyl carbon of thiazole moiety was visible at δ 18.21–18.84.

The *E* geometry of both olefinic bonds was assigned on the basis of the coupling constant (J value) between 15 and 16 Hz proving the *E*-relationship between the two olefinic protons and confirmed by the single crystal X-ray analysis of compounds **1f** and **2e**. Selected geometric parameters and ORTEP structures of these compounds are given in Table 2 and Figure 1, respectively. The torsion angles (C10—C1—C2—C3 and C1—C2—C3—C4) confirmed the overall planarity of the central α,β-unsaturated carbonyl linker, in keeping with earlier reports [18]. The data suggest limited delocalization of π-electrons density over the central chromophore despite the presence of planarity. This was seen from the length of the carbonyl bond (C1—O1), which was as expected for formal carbonyl bonds, and the double bond (C2—C3), which was typical of carbon–carbon double bonds. Angles at C1(O1—C1—C2, O1—C1—C10) and C2(C1—C2—C3) atoms deviated only marginally from the ideal angle of 120°. In contrast, significant deviations were apparent about the C3 atom (C2—C3—C4), an effect that was attributed to the presence of the C4 atom of the phenyl ring.

Table 1

Physical properties of the synthesized thiazolyl chalcone derivatives

Compounds	Thiazolylchalcone	Yield (%)
1a	R_1 = H, R_2 = Cl	82
1b	R_1 = H, R_2 = F	71
1c	R_1 = H, R_2 = CH_3	65
1d	R_1 = R_5 = H, R_3 = R_4= Cl	93
1e	R_1 = R_4 = R_5 =H, R_3 = OCH_3	96
1f	R_1 = R_3 = R_4 = H, R_5 = Br	89
2a	R_1 = CH_3, R_2 = Cl	85
2b	R_1 = CH_3, R_2 = F	69
2c	R_1 = CH_3, R_2 = CH_3	63
2d	R_1 = CH_3, R_5 = H, R_3 = R_4= Cl	97
2e	R_1 = CH_3, R_4 = R_5 = H, R_3 = OCH_3	93
2f	R_1 = CH_3, R_3 = R_4 = H, R_5 = Br	91
3a	R_1 = Br, R_2 = Cl	77
3b	R_1 = Br, R_2 = F	66
3c	R_1 = Br, R_2 = CH_3	64
3d	R_1 = Br, R_5 = H, R_3 = R_4= Cl	95
3e	R_1 = Br, R_4 = R_5 = H, R_3 = OCH_3	96
3f	R_1 = Br, R_3 = R_4 = H, R_5 = Br	92

Table 2

Selected bond lengths (Å), bonds angles (°), and torsion angles (°).

Parameters	Compound **1f**	Compound **2e**
O1—C1	1.218 (3)	1.220 (3)
C3—C4	1.465 (5)	1.462 (4)
C2—C3	1.319 (5)	1.324 (4)
C1—C2	1.467 (5)	1.474 (4)
C1—C10	1.479 (5)	1.468 (4)
C8—Br1	1.882 (4)	
O1—C1—C10	120.4 (3)	120.7 (3)
O1—C1—C2	121.1 (3)	120.8 (3)
C2—C1—C10	118.5 (3)	118.5 (3)
C1—C2—C3	121.6 (3)	121.5 (3)
C2—C3—C4	127.9 (3)	127.8 (3)
C3—C4—C5	118.6 (3)	120.2 (3)
C3—C4—C9	122.9 (3)	121.6 (3)
C3—C4—C9—C8	−179.0 (3)	179.2 (3)
C3—C4—C5—C6	179.8 (4)	−179.4 (3)
O1—C1—C2—C3	−11.1 (5)	6.4 (5)
C3—C2—C1—C10	168.7 (3)	−174.2 (3)

CONCLUSIONS

In our study, we have prepared and fully characterized a series of chalcones with thiazole and chromone moieties as pharmacophores. Facile access to these new derivatives allows for their possible exploitation for new therapies.

EXPERIMENTAL

Melting points were measured with an MPM-H1 apparatus and were uncorrected. Elemental analysis was performed with a Vario EL CHNS analyser. ^{1}H and ^{13}C NMR were recorded with a Varian Mercury-400 (400 MHz) or Varian Mercury-300 (300 MHz) NMR spectrometer in $CDCl_3$ with TMS as the internal standard. Infrared spectra were recorded with a Nicolet Avatar 360 FTIR spectrometer. Mass spectroscopy was performed Finnigan LCQ Duo spectrometer.

General procedure for the preparation of 2-aryl-4-methyl-5-acetylthiazoles. In a solution of appropriate arylthioamide (20 mmol) in ethanol (20 mL), an equimolar amount of chloroacetylacetone (20 mmol) was added. The mixture was heated under reflux for 2 h where on the solid product partially crystallized out. The reaction mixture was left to cool and the separated solid product filtered off, washed with water until absence of chlorine ion (silver nitrate test), dried, and recrystallized from ethanol to give the product in excellent purity.

2-Phenyl-4-methyl-5-acetylthiazole (1). Yield 81%; mp 65–66° C (Lit. 68–70°C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.97 (dd, J = 2 Hz and 7.9 Hz, 2H), 7.46 (m, 3H), 2.79 (s, 3H), 2.58 (s, 3H).

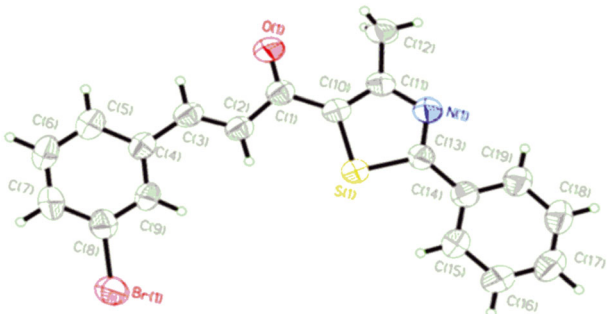
2-(p-Methylphenyl)-4-methyl-5-acetylthiazole (2). Yield 74%; mp 83–84°C (Lit. 83–84°C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ7.87 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 2.78 (s, 3H), 2.57 (s, 3H), 2.41 (s, 3H).

2-(p-Bromophenyl)-4-methyl-5-acetylthiazole (3). Yield 69%; mp 103–104°C (Lit. 102–104°C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 2.78 (s, 3H), 2.58 (s, 3H).

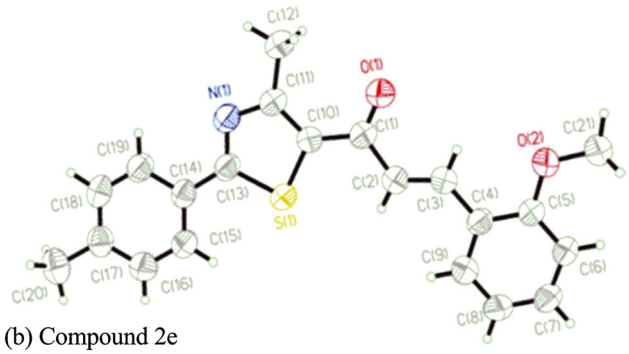
General procedure for the preparation of 1-(2′-aryl-4′-methylthiazol-5′-yl)-3-(6-chlorochromon-3-yl)-prop-2-en-1-one. 2-Aryl-4-methyl-5-acetylthyazole (1 mmol) was dissolved in ethanol (5 mL), and KOH (6*M*, 0.25 mL) was added dropwise. The appropriate 3-formylchromone (1 mmol) was added, and the reaction mixture was stirred for 12 h (reaction was monitored by TLC) at room temperature and then kept in refrigerator overnight. The excess KOH was neutralized with a solution HCl (1*M*) to give a precipitate that was filtered, washed with water, and dried. The crude was purified through column chromatography using ethyl acetate in chloroform as eluent to give the desired product in good yield.

1-(2′-Phenyl-4′-methylthiazol-5′-yl)-3-(6-chlorochromon-3-yl)-prop-2-en-1-one (1a). Yellow powder; mp 247–248°C; IR (KBr, cm^{-1}): 1664, 1652, 1595, 1559, 1465, 1360, 1328, 1292; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.47 (d, J = 15 Hz, 1H), 8.27 (d, J = 2.1 Hz, 1H), 8.19 (s, 1H), 8.02 (dd, J = 2.3 and 8 Hz, 2H), 7.65 (dd, J = 2.1 and 9 Hz, 1H), 7.45–7.49 (m, 4H), 7.41 (d, J = 15 Hz, 1H), 2.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 183.02, 175.07, 169.80, 160.62, 159.14, 153.73, 134.38, 134.33, 132.87, 132.12, 131.97, 131.17, 129.09, 129.03, 126.97, 125.76, 125.16, 119.92, 119.31, 18.83; ESI *m/z* 408 $[M+H]^+$; *Anal*. Calcd. for $C_{22}H_{14}ClNO_3S$: C, 64.78; H, 3.46; N, 3.43; S, 7.86. Found C, 64.72; H, 3.38; N, 3.45; S, 7.71.

1-(2′-Phenyl-4′-methylthiazol-5′-yl)-3-(6-fluorochromon-3-yl)-prop-2-en-1-one (1b). Yellow powder; mp 254–255°C; IR (KBr, cm^{-1}): 1664, 1647, 1595, 1559, 1479, 1362, 1326 1285; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, J = 15.2 Hz, 1H), 8.21 (s, 1H), 8.03 (dd, J = 2 Hz and 7.4 Hz, 2H), 7.95 (dd, J = 3.1 and 8.4 Hz, 1H), 7.54 (dd, J = 4.2 and 9.5 Hz, 1H), 7.46–7.48



(a) Compound 1f



(b) Compound 2e

Figure 1. ORTEP diagram of compounds (a) **1f** and (b) **2e**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

(m, 3H), 7.44 (d, *J* = 15.2 Hz, 1H), 7.42 (d, *J* = 3.1 Hz, 1H), 2.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.07, 161.66, 160.64, 159.27, 158.37, 151.64, 134.49, 132.89, 131.17, 129.09, 128.92, 126.97, 122.61, 122.28, 120.46, 120.35, 118.64, 111.42, 111.10, 18.84; ESI *m/z* 392 $[M+H]^+$; *Anal*. Calcd. for $C_{22}H_{14}FNO_3S$: C, 67.51; H, 3.61; N, 3.58; S, 8.19. Found C, 67.43; H, 3.58; N, 3.56; S, 8.15.

1-(2′-Phenyl-4′-methylthiazol-5′-yl)-3-(6-methylchromon-3-yl)-prop-2-en-1-one (1c). Yellow powder; mp 237–238°C; IR (KBr, cm^{-1}): 1664, 1647, 1591, 1565, 1483, 1366, 1327, 1297; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.45 (d, *J* = 14.8 Hz, 1H), 8.14 (s, 1H), 7.99–8.06 (m, 3H), 7.37–7.45 (m, 6H), 2.88 (s, 3H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.22, 176.35, 169.65, 160.37, 159.25, 153.70, 136.16, 135.36, 135.17, 132.93, 132.04, 131.09, 129.06, 128.36, 126.94, 125.61, 123.90, 119.03, 117.93, 21.04, 18.21; ESI *m/z* 388 $[M+H]^+$; *Anal*. Calcd. for $C_{23}H_{17}NO_3S$: C, 71.30; H, 4.42; N, 3.62; S, 8.28. Found C, 70.93; H, 4.53; N, 3.60; S, 8.23.

1-(2′-(p-Methylphenyl)-4′-methylthiazol-5′-yl)-3-(6-chlorochromon-3-yl)-prop-2-en-1-one (2a). Yellow powder; mp 227–228°C; IR (KBr, cm^{-1}): 1664, 1651, 1591, 1562, 1467, 1362, 1326, 1293; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.42 (d, *J* = 15.2 Hz, 1H), 8.25 (d, *J* = 2 Hz, 1H), 8.17 (s, 1H), 7.91 (d, *J* = 7.6 Hz, 2H), 7.65 (dd, *J* = 2.1 and 9 Hz, 1H), 7.46 (d, *J* = 9 Hz, 1H), 7.39 (d, *J* = 15.2 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 2H), 2.89 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 182.98, 175.09, 170.10, 160.58, 159.11, 153.73, 141.79, 134.38, 134.22, 132.10, 131.40, 130.18, 129.80, 129.10, 126.94, 125.77, 125.16, 119.93, 119.33, 21.56, 18.83; ESI *m/z* 420 $[M—H]^-$; *Anal.* Calcd. for $C_{23}H_{16}ClNO_3S$: C, 65.48; H, 3.82; N, 3.32; S, 7.60. Found C, 65.17; H, 4.07; N, 3.30; S, 7.56.

1-(2′-(p-Methylphenyl)-4′-methylthiazol-5′-yl)-3-(6-fluorochromon-3-yl)-prop-2-en-1-one (2b). Yellow powder; mp 255–256°C; IR (KBr, cm^{-1}): 1668, 1647, 1596, 1475, 1450, 1362, 1325, 1289; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.42 (d, *J* = 15 Hz, 1H), 8.19 (s, 1H), 7.94 (d, *J* = 2.7 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.52 (dd, *J* = 2.7 and 9 Hz, 1H), 7.45 (d, *J* = 9 Hz, 1H), 7.39 (d, *J* = 15 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 2H), 2.90 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.02, 175.45, 170.07, 161.64, 160.64, 159.24, 158.35, 151.62, 141.75, 134.37, 130.21, 129.78, 128.98, 126.91, 122.59, 122.25, 120.45, 118.65, 111.40, 21.55, 18.82; ESI *m/z* 428 $[M+Na]^+$; *Anal*. Calcd. for $C_{23}H_{16}FNO_3S$: C, 68.13; H, 3.98; N, 3.45; S, 7.91. Found C, 67.80; H, 4.13; N, 3.44; S, 7.87.

1-(2′-(p-Methylphenyl)-4′-methylthiazol-5′-yl)-3-(6′-methylchromon-3′-yl)-prop-2-en-1-one (2c). Yellow powder; mp 214–215°C; IR (KBr, cm^{-1}): 1664, 1655, 1595, 1559, 1487, 1362, 1330, 1298; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.48 (d, *J* = 15.2 Hz, 1H), 8.17 (s, 1H), 8.09 (d, *J* = 2 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.52 (dd, *J* = 2 and 8 Hz, 1H), 7.43 (d, *J* = 15.2 Hz, 1H), 7.39 (d, *J* = 8 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 2.89 (s, 3H), 2.48 (s, 3H) 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.18, 176.35, 169.92, 160.39, 159.19, 153.71, 141.63, 136.14, 135.34, 135.00, 131.58, 130.30, 129.76, 128.46, 126.88, 125.62, 123.91, 119.06, 117.93, 21.54, 21.04, 18.83; ESI *m/z* 424 $[M+Na]^+$; *Anal.* Calcd. for $C_{24}H_{19}NO_3S$: C, 71.80; H, 4.77; N, 3.49; S, 7.99. Found C, 71.44; H, 4.61; N, 3.42; S, 7.82.

1-(2′-(p-Bromophenyl)-4′-methylthiazol-5′-yl)-3-(6-chlororochromon-3-yl)-prop-2-en-1-one (3a). Yellow powder; mp 245–246°C; IR (KBr, cm^{-1}): 1668, 1647, 1591, 1563, 1498, 1362, 1329, 1294; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.36 (d, *J* = 15.2 Hz, 1H), 8.20 (s, 1H), 8.18 (d, *J* = 2 Hz, 1H), 7.82 (d, *J* = 8 Hz, 2H), 7.61 (dd, *J* = 2 and 8.8 Hz, 1H), 7.53 (d, *J*= 8 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.37 (d, *J* = 15.2 Hz, 1H), 2.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.16, 176.12, 169.13, 161.31, 159.38, 153.76, 136.33, 135.76, 132.32, 132.11, 131.81, 129.63, 128.79, 128.32, 126.86, 125.32, 123.92, 120.48, 113.53, 18.83; ESI *m/z* 486 $[M–H]^-$; *Anal*. Calcd. for $C_{22}H_{13}BrClNO_3S$: C, 54.28; H, 2.69; N, 2.88; S, 6.58. Found C, 54.06; H, 2.75; N, 2.94; S, 6.74.

1-(2′-(p-Bromophenyl)-4′-methylthiazol-5′-yl)-3-(6-fluorochromon-3-yl)-prop-2-en-1-one (3b). Yellow powder; mp 240–241°C; IR (KBr, cm^{-1}): 1670, 1657, 1590, 1559, 1480, 1363, 1329, 1294; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, *J* = 15.2 Hz, 1H), 8.21 (s, 1H), 7.95 (dd, *J* = 2.8 and 8.2 Hz, 1H), 7.89 (d, *J* = 8 Hz, 2H), 7.60 (d, *J* = 8 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.47 (d, *J* = 2.8 Hz, 1H), 7.44 (d, *J* = 15.2 Hz, 1H), 2.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.10, 176.2, 168.60, 160.27, 159.27, 153.38, 138.86, 136.14, 135.07, 132.29, 131.60, 129.56, 128.21, 125.78, 123.65, 119.18, 117.83, 111.93, 18.76; ESI *m/z* 470 $[M–H]^-$; *Anal*. Calcd. for $C_{22}H_{13}BrFNO_3S$: C, 56.18; H, 2.79; N, 2.98; S, 6.80. Found C, 55.94; H, 2.85; N, 3.05; S, 6.96.

1-(2′-(p-Bromophenyl)-4′-methylthiazol-5′-yl)-3-(6-methylchromon-3-yl)-prop-2-en-1-one (3c). Yellow powder; mp 248–249°C; IR (KBr, cm^{-1}): 1665, 1656, 1591, 1562, 1483, 1374, 1322, 1294; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.50 (d, *J* = 15 Hz, 1H), 8.18 (s, 1H), 8.10 (d, *J* = 2 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.53 (dd, *J* = 2 and 8.7 Hz, 1H), 7.45 (d, *J* = 15 Hz, 1H), 7.41 (d, *J* = 8.7 Hz, 1H), 2.90 (s, 3H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.19, 176.32, 168.25, 160.43, 159.36, 153.73, 136.24, 135.43, 135.37, 132.30, 131.87, 130.30, 129.76, 128.30, 126.88, 125.63, 123.91, 119.00, 117.96, 21.06, 18.76; ESI *m/z* 466 $[M–H]^-$; *Anal*. Calcd. for $C_{23}H_{16}BrNO_3S$: C, 59.24; H, 3.46; N, 3.00; S, 6.88. Found C, 58.98; H, 3.54; N, 3.08; S, 7.04.

General procedure for the preparation of 1-(2′-aryl-4′-methylthiazol-5′-yl)-3-arylprop-2-en-1-one. 2-Aryl-4-methyl-5-acetylthyazole (1 mmol) was dissolved in of ethanol (5 mL) and KOH (6*M*, 0.25 mL) was added dropwise. The appropriate arylcarbaldehyde (1 mmol) was added and the reaction mixture was stirred for 1 h at room temperature and kept in refrigerator overnight. The excess of KOH was neutralized with a solution HCl (1*M*) to give a precipitate that was filtered, washed with water, and dried. The residue was purified by flash column chromatography on silica gel (eluent: chloroform/ethanol 7:3) to give the corresponding products.

1-(2′-Phenyl-4′-methylthiazol-5′-yl)-3-(2,6-dichlorophenyl)-prop-2-en-1-one (1d). Yellow powder; mp 157–158°C; IR (KBr, cm^{-1}): 1660, 1603, 1495, 1422, 1371, 1326, 1201; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01 (dd, *J* = 2.2 and 8 Hz, 2H), 7.92 (d, *J* = 16 Hz, 1H), 7.50 (d, *J* = 16 Hz, 1H), 7.46–7.48 (m, 3H), 7.40 (d, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 1H), 2.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 181.96, 169.71, 160.95, 137.23, 135.62, 132.70, 132.43, 131.91, 131.24, 131.13, 130.04, 129.06, 128.95, 126.92, 18.79; ESI *m/z* 374 $[M+H]^+$; *Anal*. Calcd. for $C_{19}H_{13}Cl_2NOS$: C, 60.97; H, 3.50; N, 3.74; S, 8.57. Found C, 60.83; H, 3.57; N, 3.69; S, 8.66.

1-(2′-Phenyl-4′-methylthiazol-5′-yl)-3-(2-methoxyphenyl)-prop-2-en-1-one (1e). Yellow powder; mp 123–124°C; IR (KBr, cm^{-1}): 1656, 1591, 1491, 1418, 1370, 1330; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10 (d, *J* = 15.9 Hz, 1H), 8.01 (m, 2H), 7.61 (m, 1H), 7.45–7.48 (m, 4H), 7.42 (d, *J* = 15.9 Hz, 1H), 6.97 (m, 2H), 3.94 (s, 3H), 2.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 183.32, 169.09, 159.91, 159.00, 140.14, 132.98, 132.00, 131.83, 131.05, 129.74, 129.08, 126.92, 125.41, 123.51, 120.79, 111.26, 55.57, 18.69; ESI *m/z* 336 $[M+H]^+$; *Anal*. Calcd. for $C_{20}H_{17}NO_2S$: C, 71.62; H, 5.11; N, 4.18; S, 9.56. Found C, 71.73; H, 5.17; N, 4.24; S, 9.63.

1-(2′-Phenyl-4′-methylthiazol-5′-yl)-3-(3-bromophenyl)-prop-2-en-1-one (1f). Yellow powder; mp 122–123°C; IR (KBr, cm^{-1}): 1656, 1599, 1483, 1418, 1362, 1330; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (dd, *J* = 2 and 8 Hz, 2H), 7.76 (m, 1H), 7.70 (d, *J* = 15.6 Hz, 1H), 7. 50–7.55 (m, 2H), 7.45–7.48 (m, 3H), 7.28 (t, *J* = 8.1 Hz, 1H), 7.21 (d, *J* = 15.6 Hz, 1H), 2.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ

182.02, 169.43, 160.95, 142.46, 136.56, 133.47, 132.75, 131.28, 130.91, 130.51, 129.13, 129.09, 127.35, 126.96, 125.82, 123.14, 18.78; ESI *m/z* 384 $[M+H]^+$; *Anal*. Calcd. for $C_{19}H_{14}BrNOS$: C, 59.38; H, 3.67; N, 3.64; S, 8.34. Found C, 59.33; H, 3.70; N, 3.67; S, 8.532.

Crystal structure of 1f. $C_{19}H_{14}BrNOS$, $M = 384.28$, crystallizes as transparent yellow needle, crystal size 1.00 × 0.20 × 0.20 mm, Monoclinic, $a = 5.1723$ (5), $b = 17.8504$ (17), $c = 18.1779$ (17) Å, $\alpha = 90.00°$, $\beta = 95.59°$(10), $\gamma = 90.00°$, $V = 1670.3$ (3) $Å^3$, space group P2(1), $\mu = 2.589$ mm^{-1}, $Z = 4$, $d_{calc} = 1.528$ Mg m^{-3}, final conventional $R = 0.0330$ and $R_w = 0.0498$ for 17,001 reflections, Goodness of fit = 0.960. The crystal structure has been deposited with the Cambridge Crystallographic Data Center under the number CCDC 801763.

1-(2′-(p-Methylphenyl)-4′-methylthiazol-5′-yl)-3-(2,6-dichlorophenyl)-prop-2-en-1-one (2d). Yellow powder; mp 167–168°C; IR (KBr, cm^{-1}): 1660, 1603, 1495, 1430, 1374, 1326; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.89 (d, $J = 7.6$ Hz, 2H), 7.48 (d, $J = 15.6$ Hz, 1H), 7.38 (d, $J = 7.6$ Hz, 2H), 7.25–7.26 (m, 3H), 7.22 (d, $J = 15.6$ Hz, 1H), 2.87 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 182.04, 169.34, 161.03, 141.85, 137.23, 135.37, 132.64, 131.91, 131.20, 130.00, 129.79, 128.94, 128.26, 126.92, 21.56, 18.80; ESI *m/z* 388 $[M+H]^+$; *Anal*. Calcd. for $C_{20}H_{15}Cl_2NOS$: C, 61.86; H, 3.89; N, 3.61; S, 8.26. Found C, 61.72; H, 3.91; N, 3.80; S, 8.31.

1-(2′-(p-Methylphenyl)-4′-methylthiazol-5′-yl)-3-(2-methoxyphenyl)-prop-2-en-1-one (2e). Yellow cristal; mp 151–152°C; IR (KBr, cm^{-1}): 1656, 1591, 1491, 1434, 1370, 1330; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.11 (d, $J = 15.6$ Hz, 1H), 7.90 (d, $J = 7.6$ Hz, 2H), 7.60 (m, 1H), 7.41 (d, $J = 15.6$ Hz, 1H), 7.38 (m, 1H), 7.27 (d, $J = 7.6$ Hz, 2H), 6.98 (m, 2H), 3.94 (s, 3H), 2.87 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 183.28, 169.35, 159.90, 158.98, 141.58, 139.96, 131.94, 131.38, 130.34, 129.76, 129.68, 126.85, 125.49, 123.56, 120.77, 111.25, 55.57, 21.54, 18.70; ESI *m/z* 350 $[M+H]^+$; *Anal*. Calcd. for $C_{21}H_{19}NO_2S$: C, 72.18; H, 5.48; N, 4.01; S, 9.18. Found C, 72.26; H, 5.49; N, 4.12; S, 9.31.

Crystal structure of 2e. $C_{21}H_{19}NO_2S$, $CHCl_3$, M = 349.43, crystallizes as transparent yellow prisms, crystal size 0.40 × 0.30 × 0.20 mm, Monoclinic, $a = 13.530$ (2), $b = 12.715$ (19), $c = 10.888$ (17) Å, $\alpha = 90.00°$, $\beta = 109.16°$ (2), $\gamma = 90.00°$, $V = 1769.3$ (5) $Å^3$, space group P2(1)/*c*, $\mu = 0.197$ mm^{-1}, $Z = 4$, $d_{calc} = 1.312$ Mg m^{-3}, final conventional $R = 0.0459$ and $R_w = 0.0920$ for 5333 reflections, Goodness of fit = 1.011. The crystal structure has been deposited with the Cambridge Crystallographic Data Center under the number CCDC797369.

1-(2′-(p-Methylphenyl)-4′-methylthiazol-5′-yl)-3-(3-bromophenyl)-prop-2-en-1-one (2f). Yellow powder; mp 149–151°C; IR (KBr, cm^{-1}): 1656, 1599, 1491, 1434, 1370, 1326; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.89 (d, $J = 8.1$ Hz, 2H), 7.75 (m, 1H), 7.69 (d, $J = 15$ Hz, 1H), 7. 50–7.54 (m, 2H), 7.29 (t, $J = 7.6$ Hz, 1H), 7.26 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 15$ Hz, 1H), 2.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 181.98, 169.70, 160.97, 142.29, 141.86, 136.61, 133.42, 130.85, 130.49, 130.46, 130.11, 129.82, 127.33, 126.90, 125.91, 123.12, 21.57, 18.78; ESI *m/z* 398 $[M+H]^+$; *Anal*. Calcd. for $C_{20}H_{16}BrNOS$: C, 60.31; H, 4.05; N, 3.52; S, 8.05. Found C, 60.34; H, 4.09; N, 3.48; S, 8.16.

1-(2′-(p-Bromophenyl)-4′-methylthiazol-5′-yl)-3-(2,6-dichlorophenyl)-prop-2-en-1-one (3d). Yellow powder; mp 196–197°C; IR (KBr, cm^{-1}): 1648, 1599, 1495, 1426, 1370, 1330; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.92 (d, $J = 15.8$ Hz, 1H), 7.86 (d, $J = 8.6$ Hz, 2H), 7.58 (d, $J = 8.6$ Hz, 2H), 7.46 (d, $J = 15.8$ Hz, 1H), 7.39 (d, $J = 8$ Hz, 2H), 7.23 (t, $J = 8$ Hz, 1H), 2.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 182.05, 168.38, 161.03, 137.58, 135.39, 132.36, 132.32, 131.96, 131.68, 130.11, 128.98, 128.32, 127.88, 125.77, 18.73; ESI *m/z* 451 $[M+H]^+$; *Anal*. Calcd. for $C_{19}H_{12}BrCl_2NOS$: C, 50.36; H, 2.67; N, 3.09; S, 7.06. Found C, 50.57; H, 2.73; N, 3.18; S, 6.97.

1-(2′-(p-Bromophenyl)-4′-methylthiazol-5′-yl)-3-(2-methoxyphenyl)-prop-2-en-1-one (3e). Yellow powder; mp 176–177°C; IR (KBr, cm^{-1}): 1656, 1591, 1487, 1434, 1370, 1330; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.09 (d, $J = 15.3$ Hz, 1H), 7.86 (d, $J = 7.8$ Hz, 2H), 7.58 (d, $J = 7.8$ Hz, 2H), 7.41 (d, $J = 15.3$ Hz, 1H), 7.37 (m, 2H), 6.98 (m, 2H), 3.92 (s, 3H), 2.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 183.13, 167.61, 159.88, 159.00, 140.32, 132.27, 132.17, 132.09, 131.86, 129.76, 128.24, 125.48, 125.16, 123.40, 120.79, 111.26, 55.56, 18.64; ESI *m/z* 414 $[M+H]^+$; *Anal*. Calcd. for $C_{20}H_{16}BrNO_2S$: C, 57.98; H, 3.89; N, 3.38; S, 7.74. Found C, 57.82; H, 3.94; N, 3.43; S, 7.59.

1-(2′-(p-Bromophenyl)-4′-methylthiazol-5′-yl)-3-(3-bromophenyl)-prop-2-en-1-one (3f). Yellow powder; mp 158–159°C; IR (KBr, cm^{-1}): 1656, 1603, 1499, 1426, 1370, 1326; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.84 (d, $J = 8.4$ Hz, 2H), 7.75 (m, 1H), 7.67 (d, $J = 15.3$ Hz, 1H), 7.56 (d, $J = 8.4$ Hz, 2H), 7.51 (m, 2H), 7.27 (t, $J = 7.8$ Hz, 1H), 7.17 (d, $J = 15.3$ Hz, 1H), 2.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 181.97, 168.03, 160.96, 142.71, 136.49, 133.56, 132.36, 132.31, 131.66, 130.87, 130.54, 128.29, 127.40, 127.78, 125.66, 123.16, 18.72; ESI *m/z* 464 $[M+H]^+$; *Anal*. Calcd. for $C_{19}H_{13}Br_2NOS$: C, 49.27; H, 2.83; N, 3.02; S, 6.92. Found C, 49.24; H, 2.91; N, 3.07; S, 6.85.

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