Tetrahedron 68 (2012) 1247–1252

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Highly convergent one-pot four-component regioselective synthesis of 4*H*-benzo[*f*]chromenes via annulation of β-oxodithioesters

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ARTICLE INFO

Article history:
Received 27 September 2011
Received in revised form 19 November 2011
Accepted 19 November 2011
Available online 27 November 2011

Keywords:
Four-component reaction
Indium trichloride ($InCl_3$)
Benzo[*f*]chromene
β-Oxodithioesters
Transesterification

ABSTRACT

Highly efficient regioselective protocol for the synthesis of hitherto unreported 4*H*-benzo[*f*]chromenes has been developed by one-pot four-component coupling of aromatic aldehydes, β-naphthol, β-oxodithioesters, and primary alcohols in the presence of $InCl_3$. This transformation presumably proceeds via domino Knoevenagel condensation/Michael addition/intramolecular cyclodehydration/transesterification sequence creating four new bonds and one stereocenter in a single operation. Further, alcohol plays dual role as a reactant as well as reaction medium.

1. Introduction

Molecules with chromene framework are important synthetic targets both in pharmaceutical industry as well as in academic laboratories displaying rich chemistry and numerous applications.[1,2] They are widely present as key structural motifs in many natural products, such as alkaloids, flavonoids, tocopherols, and anthocyanins.[3] Moreover, suitably substituted chromenes have been found to exert wide spectrum of biological activities, such as antibacterial, anti-inflammatory, anti-HIV, antioxidant, and analgesic properties.[4,5] In addition, 4*H*-chromenes also find applications as cosmetics, pigments,[6] biodegradable agrochemicals,[7] and potential inhibitors of EAAT1 (Excitatory amino acid transporters) and Bcl-2 (B-cell lymphoma-2) family proteins.[8] Recent SAR studies on 4*H*-chromene derivatives reveal that they have been used in the treatment of human inflammatory TNF α-mediated diseases, such as rheumatoid and psoriatic arthritis, hypertension, asthma, ischemia, and urinary incontinence.[9]

The development of chemical methodologies that provide maximum structural complexity and diversity with a minimum number of synthetic steps to assemble compounds with interesting properties is a key facet of modern drug discovery. Multicomponent reactions[10] (MCRs) have become important tools for the creation of molecular complexity and diversity with predefined functionality in chemical biology and drug discovery; due to their straightforward experimental procedures and flexible, convergent, and atom efficient nature. Although, several synthetic methods for the synthesis of 4*H*-chromenes employing various strategies have been reported,[11,12] most of them suffer from some limitations, such as low yields, poor selectivity, expensive and/or harmful catalysts, and tedious work-up. Therefore, more general, efficient, and viable routes with operational simplicity for the synthesis of chromene derivatives are very much desirable because of their importance as substructures in a broad range of natural and synthetic products, and would be of great relevance to both synthetic and medicinal chemists.

In recent years, indium trichloride emerged as a highly efficient and effective mild Lewis acid catalyst performing a variety of chemical transformations in chemo-, regio-, and stereoselective fashion due to its air and water compatibility and operational simplicity.[13] β-Oxodithioesters, which were not commercially sourced, were prepared according to reported procedures.[14] The utility of β-oxodithioesters as versatile intermediates in organic synthesis has been well recognized.[15] Recently, β-oxodithioesters have got much attention as a key intermediates in the synthesis of various important bio-active frameworks, such as dihydropyrimidinone,[16] pyridopyrimidinone,[16] pyrazole,[17] benzo[*a*]quinolizine-4-thione,[18] 2*H*-chromene-2-thione,[19] thiochromen-5-ones,[20a] and thiophenes.[20b] Therefore, as a part of our incessant research efforts with multicomponent reactions,[21] we became intrigued in scouting the use of β-oxodithioester as one of the component to develop a more generalized synthetic strategy for the construction of benzo[*f*]chromene frameworks.

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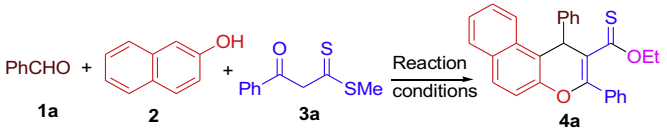
doi:10.1016/j.tet.2011.11.051

2. Results and discussion

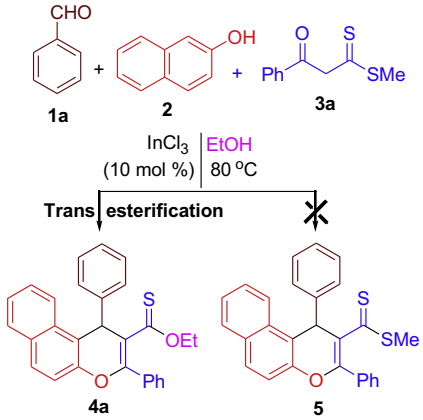
Using benzaldehyde **1a**, β-naphthol **2**, and 3-oxo-3-phenyldithiopropionic acid methyl ester **3a** in equimolar amounts as model system, a comprehensive review of reaction conditions we tested for the synthesis of benzo[*f*]chromene **4a** and are summarized in Table 1. It is worth note that, under all reaction conditions tested, we did not observe even a trace of our expected product **5**, which suggest that as the compound **5** is formed, it immediately undergoes transesterification under the reaction conditions to give benzo[*f*]chromene **4a** (Scheme 1).

Table 1
Optimization of reaction conditions for the synthesis of **4a**[a]



Entry	Catalyst (mol %)	Solvent	Time (h)	Yield[b] (%), **4a**
1	None	EtOH	6	—[c]
2	*p*-TSA (10)	EtOH	4	—[c]
3	Et_3N (10)	EtOH	4	—[c]
4	L-Proline (10)	EtOH	4	—[c]
5	$SnCl_2{\cdot}2H_2O$ (10)	EtOH	4	61
6	$CuBr_2$ (10)	EtOH	4	35
7	$InCl_3$ (10)	EtOH	4	79
8	$InCl_3$ (5)	EtOH	4	62
9	$InCl_3$ (15)	EtOH	4	77
10	$InCl_3$ (10)	CH_3CN	4	—[d]
11	$InCl_3$ (10)	THF	4	—[d]
12	$InCl_3$ (10)	H_2O	24	—[c]
13	$InCl_3$ (10)	None	6	—[c]

[a] Reaction of benzaldehyde **1a** (1 mmol), β-naphthol **2** (1 mmol), and 3-oxo-3-phenyldithiopropionic acid methyl ester **3a** (1 mmol).
[b] Isolated pure yields.
[c] No desired product.
[d] Complex reaction mixture.

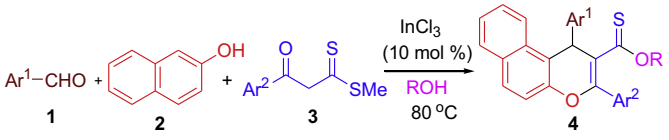


Scheme 1. Synthesis of benzo[*f*]chromene **4a**.

A control experiment verified that the reaction did not proceed in the absence of catalyst (Table 1, entry 1). Initially, the above model reaction was performed in the presence of different catalysts, such as *p*-TSA, Et_3N, L-proline, $SnCl_2{\cdot}2H_2O$, $CuBr_2$, and $InCl_3$ (10 mol % each) separately in refluxing ethanol. *p*-TSA, Et_3N, and L-proline were found to be completely ineffective (Table 1, entries 2–4). $SnCl_2{\cdot}2H_2O$ and $CuBr_2$ did catalyze the reaction to furnish the desired product **4a** albeit in low yields (Table 1, entries 5 and 6). To our delight, $InCl_3$ gave the desired benzo[*f*]chromene **4a** in 79% yield (Table 1, entry 7, Scheme 1). Encouraged by this result, we then focused on optimizing the reaction conditions. Subsequently, $InCl_3$ loading was examined (Table 1, entries 7–9), and it was found that 10 mol % of $InCl_3$ provided the maximum yield in minimum time (Table 1, entry 7). Further, the effect of different solvents, such as CH_3CN, THF, and H_2O was also investigated at their reflux temperatures in the presence of 10 mol % of $InCl_3$, which were found to be ineffective (Table 1, entries 10–12). The addition of phase transfer catalyst tetrabutyl ammonium hydrogen sulfate also did not make any difference in aqueous medium. In addition, the above test reaction was also performed under solvent-free conditions, but no desired product was obtained (Table 1, entry 13). Thus, the best yield, cleanest reaction, and most facile work-up were achieved employing 10 mol % of $InCl_3$ in refluxing ethanol.

Our literature survey at this stage revealed that there are no reports on the use of $InCl_3$ as catalyst in the synthesis of benzo[*f*]chromene derivatives by the coupling of aromatic aldehydes, β-naphthol, and β-oxodithioesters. With these results in hand, we next utilized a variety of substrates to explore the synthetic scope and generality of this cascade reaction and to generate a small library of functionalized benzo[*f*]chromenes **4**. Representative results are shown in Table 2.

Table 2
Synthesis of 4*H*-benzo[*f*]chromenes **4**



Product	Ar^1	Ar^2	R	Time (h)	Yield[a] (%)
4a	C_6H_5	C_6H_5	C_2H_5	4.0	79
4b	4-MeC_6H_4	C_6H_5	C_2H_5	3.5	65
4c	4-$NO_2C_6H_4$	C_6H_5	C_2H_5	4.0	75
4d	4-FC_6H_4	C_6H_5	C_2H_5	3.5	77
4e	C_6H_5	4-$OMeC_6H_4$	C_2H_5	3.5	71
4f	2-ClC_6H_4	4-$OMeC_6H_4$	C_2H_5	3.5	63
4g	2-$OMeC_6H_4$	4-$OMeC_6H_4$	C_2H_5	4.0	65
4h	4-OHC_6H_4	4-$OMeC_6H_4$	C_2H_5	4.5	68
4i	C_6H_5	4-ClC_6H_4	C_2H_5	3.5	83
4j	4-MeC_6H_4	4-ClC_6H_4	C_2H_5	4.5	79
4k	C_6H_5	2-Thienyl	C_2H_5	3.0	81
4l	4-$OMeC_6H_4$	2-Thienyl	C_2H_5	4.0	69
4m	3-ClC_6H_4	2-Thienyl	C_2H_5	3.5	68
4n	4-MeC_6H_4	2-Thienyl	C_2H_5	3.0	75
4o	C_6H_5	C_6H_5	CH_3	4.0	58
4p	C_6H_5	2-Thienyl	CH_3	3.0	65
4q	C_6H_5	4-$OMeC_6H_4$	CH_3	4.0	76
4r	C_6H_5	C_6H_5	*n*-C_4H_9	4.5	63
4s	C_6H_5	2-Thienyl	*n*-C_4H_9	4.5	68
4t	C_6H_5	C_6H_5	*i*-Pr	6.0	0

[a] Isolated yields.

Notably, a wide range of aromatic aldehydes bearing electron-withdrawing as well as electron-donating groups and various β-oxodithioesters were well tolerated, and proceeded smoothly under the optimized reaction conditions. Further, to expand the scope of this protocol and to gain more clear insight into the reaction, we also carried out the above test reaction in different alcohols, such as MeOH, *n*-BuOH, and *i*-PrOH (Table 2, products **4o**–**t**). Primary alcohols provided the products in moderate to good yields, whereas sterically hindered secondary alcohol *i*-PrOH did not provide any trace of the desired product, but it led to a complex mixture of several very close spots on the TLC plate, which could not be isolated, thus limiting the scope of the reaction to some extent.

The structures of all the newly synthesized compounds were well characterized from their satisfactory elemental and spectral (IR, ^1H, ^{13}C NMR, and mass) studies. The mass spectra of these

compounds displayed molecular ion peaks at the appropriate *m*/*z* values. Finally, the structure of one representative compound 2-(4-chlorophenyl)-4-phenyl-4*H*-benzo[*f*]chromene-3-carbothioic acid *O*-ethyl ester **4i** was confirmed unambiguously by the X-ray single crystal diffraction analysis (Fig. 1).[22]

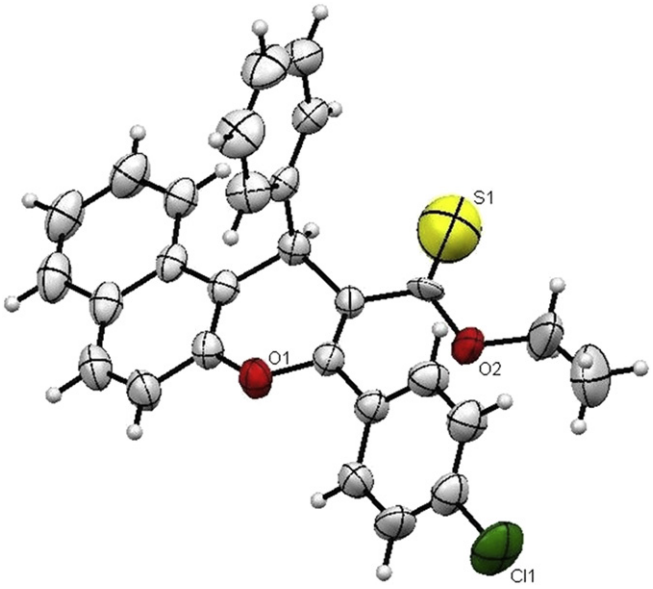
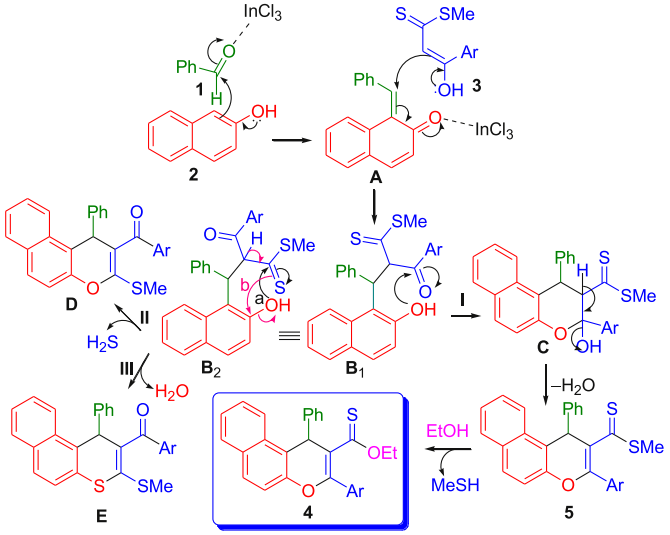


Fig. 1. ORTEP diagram of the compound **4i**.

Although we have not established the mechanism of the reaction experimentally, on the basis of above results, a plausible reaction scenario for the formation of benzo[*f*]chromenes is outlined in Scheme 2. The reaction is supposed to proceed via the



Scheme 2. A plausible mechanism for the formation of benzo[*f*]chromene **4**.

Michael acceptor *ortho*-quinonemethide intermediate (*o*-QM) **A**, formed by the nucleophilic addition of β-naphthol **2** to aldehyde **1**. *ortho*-quinonemethide intermediate **A** is highly reactive and could not be isolated at room temperature. The enol form of β-oxodithioester **3** attacks to **A** in a Michael-type fashion to produce an open chain intermediate $\mathbf{B_1}$. $\mathbf{B_1}$ undergoes regiospecific O-cyclization via route **I** followed by dehydration to give the benzo[*f*]chromene **5**, which could not be isolated and immediately undergoes transesterification by the alcohol under the reaction conditions to give benzo[*f*]chromene **4**. The alternative rotamer $\mathbf{B_2}$ may undergo cyclization via its two different routes **II** and **III** to furnish benzo[*f*]chromene **D** and benzo[*f*]thiochromene **E**, respectively. During our investigation, we did not observe a trace of **D** and **E**, and only **4** was obtained exclusively thus, making this protocol highly regioselective. This operationally simple and four-component domino process concomitantly created two new C–C and two C–O bond leading to chromene ring.

3. Conclusion

In summary, we have developed an efficient and highly convergent one-pot four-component domino protocol for the synthesis of functionalized benzo[*f*]chromenes in refluxing alcohol promoted by $InCl_3$ for the first time. It should be noted that alcohol plays dual role as a reactant as well as reaction medium. This transformation proceeds via Knoevenagel condensation/Michael addition/intramolecular cyclodehydration/transesterification sequence creating four new bonds in highly chemo- and regioselective manner and one stereocenter in a single operation. This method not only provides an excellent complement to benzo[*f*]chromenes synthesis, but also avoids the use of hazardous reagents.

4. Experimental section

4.1. General

All starting materials were used as received without further purification. β-Oxodithioesters were prepared following known procedure.[14] Thin-layer chromatography (TLC) was performed using silica gel 60 F_{254} precoated plates. Infrared (IR) spectra are measured in KBr, and wavelengths (ν) are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on NMR spectrometers operating at 300 MHz, 200 MHz, and 75 MHz, 50 MHz, respectively. Chemical shifts (δ) are given in parts per million (ppm) using the residue solvent peaks as reference relative to TMS. *J* values are given in hertz. Mass spectra were recorded using electro spray ionization (ESI) mass spectrometry. The C, H, and N analysis were performed from micro analytical laboratory. The melting points are uncorrected.

4.2. General procedure for the synthesis of 4*H*-benzo[*f*]chromene-3-carbothioic acid *O*-ethyl ester (4)

A mixture of aldehyde (1.0 mmol), β-naphthol (1.0 mmol), and β-oxodithioester (1.0 mmol) was placed in a 25 mL round bottom flask containing 2 mL dry ethanol. $InCl_3$ (22 mg, 10 mmol) was added to it and the reaction mixture was heated at 80 °C for the stipulated period of time. After completion of the reaction (monitored by TLC) ethanol was evaporated under reduced pressure. The residue thus obtained was diluted with water (20 mL) and extracted with ethyl acetate (2×10 mL). The combined organic extract was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum and the residue was purified by column chromatography over silica gel using ethyl acetate and *n*-hexane mixture (1:49) as eluent, which afforded the desired product in excellent purity. The physical and spectral data of the synthesized compounds are as follows.

*4.2.1. 2,4-Diphenyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4a**).* Colorless jelly; IR (KBr, ν_{max}, cm^{-1}): 3065, 1705, 1059; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.11 (d, J=8.4 Hz, 2H), 7.89–7.81 (m, 3H), 7.63–7.59 (m, 2H), 7.46–7.37 (m, 9H), 5.87 (s, 1H), 3.99 (q, J=7.2 Hz, 2H), 0.91 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 166.9, 159.4, 152.2, 148.2, 146.6, 134.7, 131.5, 130.6, 129.9, 129.6, 129.2, 128.8, 128.7, 127.9, 127.3, 125.0,

123.8, 122.6, 117.2, 115.6, 107.0, 60.5, 39.1, 13.5; ESI-MS: m/z=423.1 (M^++1). Anal. Calcd for $C_{28}H_{22}O_2S$: C, 79.59; H, 5.25. Found: 79.87; H, 5.45.

*4.2.2. 2-Phenyl-4-p-tolyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4b**).* Pale yellow jelly; IR (KBr, ν_{max}, cm^{-1}): 3066, 1702, 1065; ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 8.00 (d, J=7.2 Hz, 1H), 7.80–7.73 (m, 2H), 7.68–7.45 (m, 4H), 7.41–7.17 (m, 4H), 7.14–6.95 (m, 4H), 5.72 (s, 1H), 4.18 (q, J=7.2 Hz, 2H), 2.25 (s, 3H), 1.18 (t, J=7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, δ ppm): 167.3, 151.1, 148.3, 141.9, 136.4, 135.6, 131.6, 131.0, 130.6, 130.1, 129.8, 129.4, 128.9, 128.7, 128.5, 128.3, 127.9, 127.1, 126.8, 126.5, 124.9, 123.6, 123.3, 117.4, 108.9, 60.8, 39.5, 21.1, 14.0; ESI-MS: m/z=437.1 (M^++1). Anal. Calcd for $C_{29}H_{24}O_2S$: C, 79.78; H, 5.54. Found: C, 80.04; H, 5.69.

*4.2.3. 4-(4-Nitrophenyl)-2-phenyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4c**).* Pale yellow jelly; IR (KBr, ν_{max}, cm^{-1}): 3069, 1704, 1062; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.02 (d, J=8.4 Hz, 1H), 7.80–7.74 (m, 2H), 7.48–7.34 (m, 9H), 7.24–7.20 (m, 2H), 7.13–7.09 (m, 1H), 5.76 (s, 1H), 3.98 (q, J=8.1 Hz, 2H), 0.94 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.1, 158.2, 148.2, 145.1, 135.1, 131.4, 130.9, 129.4, 128.8, 128.6, 128.4, 128.3, 127.9, 127.7, 126.9, 126.8, 126.5, 124.6, 123.2, 117.1, 116.9, 108.3, 60.2, 39.1, 13.5; ESI-MS: m/z=468.2 (M^++1). Anal. Calcd for $C_{28}H_{21}NO_4S$: C, 71.93; H, 4.53; N, 3.00. Found: C, 71.70; H, 4.79; N, 3.12.

*4.2.4. 4-(4-Fluorophenyl)-2-phenyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4d**).* Pale brown jelly; IR (KBr, ν_{max}, cm^{-1}): 3067, 1701, 1058; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.96 (d, J=8.4 Hz, 1H), 7.81–7.75 (m, 2H), 7.50–7.34 (m, 10H), 6.93–6.88 (m, 2H), 5.75 (s, 1H), 3.99 (q, J=6.9 Hz, 2H), 0.93 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.1, 158.3, 148.1, 140.9, 135.0, 131.4, 130.7, 129.8, 129.7, 129.6, 128.8, 128.5, 127.8, 126.9, 124.8, 123.0, 117.2, 116.7, 115.4, 115.1, 108.1, 60.3, 38.4, 13.5; ESI-MS: m/z=441.2 (M^++1). Anal. Calcd for $C_{28}H_{21}FO_2S$: C, 76.34; H, 4.80. Found: C, 76.59; H, 4.95.

*4.2.5. 2-(4-Methoxyphenyl)-4-phenyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4e**).* Pale yellow jelly; IR (KBr, ν_{max}, cm^{-1}): 3057, 1700, 1066; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.02 (d, J=8.4 Hz, 1H), 7.79–7.73 (m, 2H), 7.48–7.34 (m, 6H), 7.23–7.19 (m, 3H), 7.12 (d, J=7.2 Hz, 1H), 6.93 (d, J=8.4 Hz, 2H), 5.73 (s, 1H), 4.04 (q, J=7.2 Hz, 2H), 3.83 (s, 3H), 1.03 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.3, 160.7, 158.4, 148.2, 145.2, 130.6, 128.7, 128.4, 128.2, 126.8, 126.5, 124.6, 123.1, 117.2, 113.1, 107.3, 60.3, 55.3, 39.2, 14.1; ESI-MS: m/z=453.2 (M^++1). Anal. Calcd for $C_{29}H_{24}O_3S$: C, 76.96; H, 5.35. Found: C, 77.19; H, 5.49.

*4.2.6. 4-(2-Chlorophenyl)-2-(4-methoxyphenyl)-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4f**).* Pale yellow jelly; IR (KBr, ν_{max}, cm^{-1}): 3057, 1701, 1059; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.24 (d, J=8.1 Hz, 1H), 7.95–7.74 (m, 2H), 7.50 (d, J=8.7 Hz, 3H), 7.36–7.31 (m, 4H), 7.09–7.04 (m, 2H), 6.94 (d, J=8.7 Hz, 2H), 6.12 (s, 1H), 4.04 (q, J=5.4 Hz, 2H), 3.85 (s, 3H), 1.05 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.3, 160.7, 148.3, 143.0, 132.0, 131.7, 131.3, 131.2, 130.3, 129.6, 129.0, 128.4, 127.8, 127.5, 127.0, 124.7, 123.5, 117.3, 113.3, 107.2, 60.5, 55.4, 36.1, 13.8; ESI-MS: m/z=487.1 (M^++1). Anal. Calcd for $C_{29}H_{23}ClO_3S$: C, 71.52; H, 4.76. Found: C, 71.79; H, 4.66.

*4.2.7. 2-(4-Methoxyphenyl)-4-(2-methoxyphenyl)-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4g**).* Pale yellow jelly. IR (KBr, ν_{max}, cm^{-1}): 3057, 1699, 1067; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.27 (d, J=8.4 Hz, 1H), 7.76–7.68 (m, 2H), 7.49–7.44 (m, 3H), 7.37–7.29 (m, 3H), 7.09 (d, J=7.2 Hz, 1H), 6.94–6.81 (m, 4H), 6.08 (s, 1H), 3.98–3.91 (m, 5H), 3.84 (s, 3H), 1.02 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.1, 160.5, 158.0, 155.9, 148.3, 133.8, 131.4, 131.1, 130.5, 130.4, 128.3, 127.8, 126.6, 124.4, 123.5, 121.0, 117.8, 117.2, 113.2, 110.9, 107.1, 60.1, 55.5, 55.3, 32.9, 14.1; ESI-MS: m/z=483.1 (M^++1). Anal. Calcd for $C_{30}H_{26}O_4S$: C, 74.66; H, 5.43. Found: C, 74.83; H, 5.59.

*4.2.8. 4-(4-Hydroxypheyl)-2-(4-methoxyphenyl)-4H-benzo[f] chromene-3-carbothioic acid O-ethyl ester (**4h**).* Yellow jelly; IR (KBr, ν_{max}, cm^{-1}): 3599, 3070, 1702, 1067; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.00 (d, J=8.4 Hz, 1H), 7.80–7.73 (m, 2H), 7.47 (d, J=8.4 Hz, 3H), 7.37–7.33 (m, 1H), 7.29–7.25 (m, 3H), 6.93 (d, J=8.4 Hz, 2H), 6.67 (d, J=8.4 Hz, 2H), 5.66 (s, 1H), 4.72 (s, 1H), 4.04 (q, J=7.2 Hz, 2H), 3.84 (s, 3H), 1.03 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.6, 160.7, 158.2, 154.1, 148.1, 137.7, 131.4, 130.9, 130.6, 129.4, 128.6, 128.4, 127.3, 126.8, 124.6, 123.2, 117.4, 117.2, 115.2, 113.1, 107.5, 60.3, 55.3, 38.3, 13.8; ESI-MS: m/z=469.2 (M^++1). Anal. Calcd for $C_{29}H_{24}O_4S$: C, 74.34; H, 5.16. Found: C, 73.59; H, 5.34.

*4.2.9. 2-(4-Chlorophenyl)-4-phenyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4i**).* Yellow solid; mp 174–175 °C; IR (KBr, ν_{max}, cm^{-1}): 3059, 1700, 1065; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.01 (d, J=8.4 Hz, 1H), 7.80–7.52 (m, 2H), 7.46–7.32 (m, 9H), 7.24–7.20 (m, 2H), 7.14–7.09 (m, 1H), 5.75 (s, 1H), 4.02 (q, J=7.2 Hz, 2H), 1.02 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 166.7, 157.1, 148.0, 144.9, 135.5, 133.5, 131.4, 130.8, 130.3, 128.9, 128.4, 128.3, 128.0, 126.9, 126.6, 124.7, 123.2, 117.0, 116.8, 108.6, 60.5, 39.1, 13.6; ESI-MS: m/z=457.1 (M^++1). Anal. Calcd for $C_{28}H_{21}ClO_2S$: C, 73.59; H, 4.63. Found: C, 73.95; H, 4.39.

*4.2.10. 2-(4-Chlorophenyl)-4-p-tolyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4j**).* Pale brown solid; mp 170–171 °C; IR (KBr, ν_{max}, cm^{-1}): 3065, 1703, 1065; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.01 (d, J=8.4 Hz, 1H), 7.80–7.74 (m, 2H), 7.45–7.28 (m, 9H), 7.04 (d, J=7.5 Hz, 2H), 5.71 (s, 1H), 4.02 (q, J=6.9 Hz, 2H), 2.23 (s, 3H), 1.02 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 166.8, 157.0, 148.0, 142.0, 136.2, 135.5, 133.6, 131.4, 130.9, 130.4, 129.2, 128.8, 128.4, 128.1, 128.0, 126.9, 124.7, 123.2, 117.0, 108.8, 60.4, 38.7, 21.0, 13.7; ESI-MS: m/z=471.2 (M^++1). Anal. Calcd for $C_{29}H_{23}ClO_2S$: C, 73.95; H, 4.92. Found: C, 73.61; H, 5.09.

*4.2.11. 4-Phenyl-2-thienyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4k**).* Red jelly; IR (KBr, ν_{max}, cm^{-1}): 3065, 1702, 1065; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.98 (d, J=8.1 Hz, 1H), 7.81–7.76 (m, 2H), 7.52–7.37 (m, 7H), 7.24–7.19 (m, 2H), 7.14–7.05 (m, 2H), 5.74 (s, 1H), 4.16 (q, J=7.2 Hz, 2H), 1.17 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.0, 150.9, 148.1, 144.5, 135.3, 131.4, 130.8, 130.5, 128.8, 128.6, 128.5, 128.3, 128.2, 127.0, 126.9, 126.6, 124.7, 123.1, 117.1, 117.0, 108.4, 60.6, 39.6, 13.8; ESI-MS: m/z=429.1 (M^++1). Anal. Calcd for $C_{26}H_{20}O_2S_2$: C, 72.87; H, 4.70. Found: C, 72.61; H, 4.88.

*4.2.12. 4-(4-Methoxyphenyl)-2-thienyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4l**).* Red jelly; IR (KBr, ν_{max}, cm^{-1}): 3067, 1699, 1067; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.97 (d, J=8.4 Hz, 1H), 7.84–7.74 (m, 3H), 7.51–7.35 (m, 4H), 7.31–7.24 (m, 1H), 7.07–6.98 (m, 2H), 6.76 (d, J=8.7 Hz, 2H), 5.69 (s, 1H), 4.16 (q, J=7.2 Hz, 2H), 3.70 (s, 3H), 1.16 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.1, 158.2, 148.0, 147.6, 147.0, 131.9, 130.4, 129.2, 128.7, 128.5, 128.3, 126.8, 126.6, 124.7, 124.4, 123.9, 119.0, 117.1, 114.2, 113.8, 60.6, 55.1, 38.8, 14.1; ESI-MS: m/z=459.1 (M^++1). Anal. Calcd for $C_{27}H_{22}O_3S_2$: C, 70.71; H, 4.84. Found: C, 70.99; H, 4.99.

*4.2.13. 4-(3-Chlorophenyl)-2-thienyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4m**).* Pale yellow jelly; IR (KBr, ν_{max}, cm^{-1}): 1067, 1702, 1065; ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.92 (d, J=8.1 Hz, 1H), 7.83–7.78 (m, 2H), 7.54–7.48 (m, 2H), 7.41–7.7.37

(m, 3H), 7.25–7.24 (m, 1H), 7.14–7.06 (m, 4H), 5.73 (s, 1H), 4.18 (q, J=7.2 Hz, 2H), 1.19 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 166.8, 151.5, 148.1, 146.5, 134.2, 131.4, 130.8, 129.7, 129.2, 128.6, 128.3, 127.8, 127.1, 127.0, 126.8, 126.4, 124.9, 122.8, 117.1, 116.2, 107.6, 60.8, 39.3, 13.8; ESI-MS: m/z=463.1 (M^++1). Anal. Calcd for $C_{26}H_{19}ClO_2S_2$: C, 67.45; H, 4.14. Found: C, 67.67; H, 4.36.

*4.2.14. 2-Thienyl-4-p-tolyl-4H-benzo[f]chromene-3-carbothioic acid O-ethyl ester (**4n**).* Red jelly; IR (KBr, ν_{max}, cm^{-1}): 3062, 1701, 1067; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.99 (d, J=8.4 Hz, 1H), 7.79–7.74 (m, 2H), 7.51–7.36 (m, 5H), 7.29–7.24 (m, 2H), 7.07–7.00 (m, 3H), 5.70 (s, 1H), 4.15 (q, J=6.9 Hz, 2H), 2.22 (s, 3H), 1.17 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.1, 150.9, 148.0, 141.7, 136.2, 135.4, 131.4, 130.8, 130.5, 129.2, 128.7, 128.5, 128.3, 128.0, 126.9, 126.6, 124.7, 123.1, 117.2, 117.1, 108.6, 60.6, 39.2, 21.0, 13.8; ESI-MS: m/z=443.2 (M^++1). Anal. Calcd for $C_{27}H_{22}O_2S_2$: C, 73.27; H, 5.01. Found: C, 73.56; H, 4.89.

*4.2.15. 2,4-Diphenyl-4H-benzo[f]chromene-3-carbothioic acid O-methyl ester (**4o**).* Pale orange solid; mp 84–85 °C; IR (KBr, ν_{max}, cm^{-1}): 3065, 1703, 1065; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 8.01 (d, J=8.1 Hz, 1H), 7.80–7.75 (m, 2H), 7.51–7.34 (m, 11H), 7.23–7.20 (m, 1H), 7.14–7.09 (m, 1H), 5.76 (s, 1H), 3.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm):167.6, 145.0, 129.6, 128.8, 128.5, 128.2, 127.8, 126.9, 126.6, 124.7, 123.2, 117.2, 108.0, 97.2, 51.3, 39.2; ESI-MS: m/z=409.1 (M^++1). Anal. Calcd for $C_{27}H_{20}O_2S$: C, 79.38; H, 4.93. Found: C, 79.68; H, 4.77.

*4.2.16. 4-Phenyl-2-thienyl-4H-benzo[f]chromene-3-carbothioic acid O-methyl ester (**4p**).* Brown solid; mp 120–121 °C; IR (KBr, ν_{max}, cm^{-1}): 3065, 1701, 1065; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.98 (d, J=8.4 Hz, 1H), 7.81–7.76 (m, 2H), 7.56 (d, J=3.0 Hz, 1H), 7.49–7.37 (m, 6H), 7.22–7.06 (m, 4H), 5.75 (s, 1H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.5, 151.3, 148.1, 144.5, 135.3, 131.4, 130.8, 130.6, 128.9, 128.5, 128.1, 126.9, 126.7, 124.7, 123.1, 117.1, 109.4, 107.9, 51.6, 39.6; ESI-MS: m/z=415.1 (M^++1). Anal. Calcd for $C_{25}H_{18}O_2S_2$: C, 72.43; H, 4.38. Found: C, 72.63; H, 4.59.

*4.2.17. 2-(4-Methoxyphenyl)-4-phenyl-4H-benzo[f]chromene-3-carbothioic acid O-methyl ester (**4q**).* Yellow solid; mp 188–189 °C; IR (KBr, ν_{max}, cm^{-1}): ^{1}H NMR (200 MHz, $CDCl_3$, δ ppm): 8.00 (d, J=6.0 Hz, 1H), 7.78–7.71 (m, 2H), 7.47–7.42 (m, 2H), 7.41–7.37 (m, 2H), 7.35–7.29 (m, 2H), 7.22–7.20 (m, 2H), 7.16–7.08 (m, 2H), 6.92 (d, J=8.6 Hz, 2H), 5.71 (s, 1H), 3.82 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, δ ppm): 167.8, 160.8, 158.5, 148.2, 145.2, 131.4, 130.9, 130.6, 128.8, 128.4, 128.2, 127.0, 126.9, 126.5, 124.6, 123.2, 117.3, 117.2, 113.2, 107.1, 55.3, 51.3, 39.2; ESI-MS: m/z=439.1 (M^++1). Anal. Calcd for $C_{28}H_{22}O_3S$: C, 76.69; H, 5.06. Found: C, 76.94; H, 5.23.

*4.2.18. 2,4-Diphenyl-4H-benzo[f]chromene-3-carbothioic acid O-butyl ester (**4r**).* Pale red jelly; IR (KBr, ν_{max}, cm^{-1}): 3065, 1735, 3065; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 8.02 (d, J=7.2 Hz, 1H), 7.78–7.73 (m, 2H), 7.48–7.33 (m, 10H), 7.24–7.11 (m, 3H), 5.76 (s, 1H), 3.92 (t, J=6.0 Hz, 2H), 1.25–1.24 (m, 2H), 1.01–0.95 (m, 2H), 0.76 (t, J=6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 167.2, 158.2, 148.1, 145.1, 135.2, 131.4, 130.9, 129.4, 128.9, 128.8, 128.4, 128.3, 127.8, 126.9, 126.5, 124.6, 123.2, 117.1, 117.0, 108.3, 64.3, 39.1, 30.1, 18.9, 13.6; ESI-MS: m/z=451.2 (M^++1). Anal. Calcd for $C_{30}H_{26}O_2S$: C, 79.97; H, 5.82. Found: C, 79.62; H, 5.99.

*4.2.19. 4-Phenyl-2-thienyl-4H-benzo[f]chromene-3-carbothioic acid O-butyl ester (**4s**).* Red jelly; IR (KBr, ν_{max}, cm^{-1}): 3067, 1729, 1067; ^{1}H NMR (200 MHz, $CDCl_3$, δ ppm): 8.00 (d, J=8.2 Hz, 1H), 7.82–7.76 (m, 2H), 7.52–7.47 (m, 3H), 7.42–7.29 (m, 4H), 7.23–7.19 (m, 2H), 7.16–7.12 (m, 1H), 7.09–7.05 (m, 1H), 5.76 (s, 1H), 4.10 (t, J=6.6 Hz, 2H), 1.52–1.34 (m, 2H), 1.21–1.13 (m, 2H), 0.89 (t, J=7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, δ ppm): 167.3, 151.1, 148.3, 144.7, 135.6, 131.6, 131.0, 130.6, 129.0, 128.6, 128.3, 127.1, 126.8, 124.8, 123.3, 117.3, 108.8, 64.7, 39.8, 30.5, 19.2, 13.8; ESI-MS: m/z=457.2 (M^++1). Anal. Calcd for $C_{28}H_{24}O_2S_2$: C, 73.65; H, 5.30. Found: C, 73.93; H, 5.12.

Acknowledgements

This work was carried out under financial support from the Council of Scientific and Industrial Research (Grant 01(2260)/08/EMR-II) and the Department of Science and Technology (Grant SR/S1/OC-66/2009), New Delhi. S.S. and G.C.N. are thankful to the Council of Scientific and Industrial Research (CSIR), New Delhi, for their senior research fellowship (SRF).

Supplementary data

X-ray structure and crystallographic information file (CIF) for compound **4i**. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.11.051.

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22. Crystallographic data for compound **4i** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 835684. These data can be obtained free of charge at www.ccdc.cam.ac.uk.