Tetrahedron 70 (2014) 914–918

Contents lists available at ScienceDirect

Tetrahedron

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

Regioselective dehydrative intramolecular heteroannulation of β-allyl-β-hydroxy dithioesters: facile and straightforward entry to 2*H*-thiopyrans

Sushobhan Chowdhury [a], Tanmoy Chanda [a], Suvajit Koley [a], B. Janaki Ramulu [a], Keshav Raghuvanshi [b], Maya Shankar Singh [a,*]

[a] Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi 221005, India
[b] Institut fuer Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen, Tammannstr. 2, 37077 Goettingen, Germany

ARTICLE INFO

Article history:
Received 11 November 2013
Received in revised form 2 December 2013
Accepted 8 December 2013
Available online 12 December 2013

Keywords:
β-Allyl-β-hydroxy dithioesters
$BF_3 \cdot Et_2O$
Regioselective dehydration
Intramolecular thioannulation
Thiopyrans

ABSTRACT

β-Allyl-β-hydroxy dithioesters have been employed in the synthesis of hitherto unreported and synthetically demanding 2*H*-thiopyrans via regioselective intramolecular annulation strategy. Lewis acid $BF_3 \cdot Et_2O$ efficiently mediates the regioselective dehydration followed by intramolecular thioannulation at room temperature. The attractive features of this protocol include mild conditions, high atom-economy and excellent yields with the elimination of water as the only by-product.

1. Introduction

Thiopyrans and their derivatives are important privileged structural motifs present not only in several natural products and biologically active molecules,[1,2] but also frequently utilized as synthetic blocks in organic synthesis.[3] They have been utilized in the construction of analogues of natural products, such as tetrahydrodicranenone B,[4] serricornin,[5] thromboxanes,[6] and cyclopentanoids.[7] More specifically, compounds containing the thiopyran substructure find application in a wide variety of therapeutical areas, which includes antibacterial,[8] antihyperplasic,[9] antipsychiatric,[10] and anticancer activities.[11,12] Thiopyran derivatives have also been shown to be powerful inhibitors of deoxyribonucleic acid protein kinase.[13] For these reasons, the development of new methodologies for the regioselective synthesis of functionalized thiopyrans continues to be an active area of research in fine chemistry.

Among several elegant approaches reported in the literature to synthesize thiopyrans, the major routes typically involve the Diels–Alder cycloaddition of different functionalized dienes with activated dienophiles,[14] the coupling reaction of benzoyl(acetyl) thioacetamides with α,β-unsaturated aldehydes,[15] (3,5)-thionium-ene cyclization reaction of aldehydes and substituted 5-methylhex-4-ene-1-thiol,[16] and metathesis of sulfur containing alkenes.[17]

Although some multicomponent approaches for the synthesis of thiopyrans have been developed,[18,19] regioselective control of the functionalization of thiopyran is still the main concern. Fused thiopyran skeletons have been achieved via intramolecular hydroarylation with arene-yne substrates[20] and [4+2]-cycloaddition of active methylene compounds with *N*,*N*-dimethylformamide dimethyl acetals.[21] Albeit the reported protocols are useful tools for the construction of thiopyran frameworks, most of them suffer from significant limitations, such as harsh reaction conditions, poor yields, limited functional group tolerability and production of hazardous wastes. Therefore, a robust, practical, efficient, viable and regioselective method for the synthesis of thiopyrans with broad scope is highly desirable, and would be of great relevance to both synthetic and medicinal chemists.

Present era of organic synthesis is mainly themed on the design and development of practical cascades that provide maximum structural intricacy with economies of step, atom, cost and waste generation. It is pertinent to mention that the rich and fascinating

* Corresponding author. Tel.: +91 542 6702502; fax: +91 542 2368127; e-mail addresses: mssinghbhu@yahoo.co.in, mayashankarbhu@gmail.com (M.S. Singh).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.12.020

chemistry that stems from one-pot annulation strategy, where several bonds are formed and/or cleaved provides a robust approach for the construction of diverse molecules. In this context, intramolecular annulations are coming up with great success. Importantly, the selection of synthons to design such transformations is highly crucial that governs the success of a protocol. In our recent report,[22] we have utilized β-allyl-β-hydroxy dithioesters to generate some valuable synthetic residues, which can be further employed in different synthetic transformations. In this context, we report herein a new method for the regioselective synthesis of 2*H*-thiopyrans from β-allyl-β-hydroxy dithioesters through a cascade dehydrative intramolecular annulation sequence.

2. Results and discussion

Chemical species containing both electrophilic and nucleophilic sites have great potential in developing new reaction pathways and diverse molecular entities. One such simple polyfunctional chemical species is β-allyl-β-hydroxy dithioester with the general structure **1** (Fig. 1).

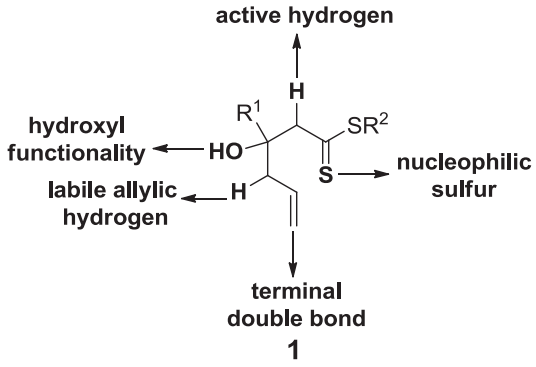
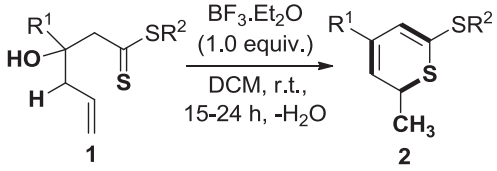


Fig. 1. Reactive sites of β-allyl-β-hydroxy dithioester **1**.

Due to the presence of several reactive sites, such as hydroxyl, allyl, active methylene and dithioester groups, β-allyl-β-hydroxy dithioesters **1** can be exploited in a regioselective manner to construct five-/six-member and fused heterocycles depending on the reaction conditions. The β-allyl-β-hydroxy dithioesters **1** are not commercially sourced, and were synthesized from the corresponding β-oxodithioesters in good yields by the regioselective Grignard addition[22,23] (Scheme 1).

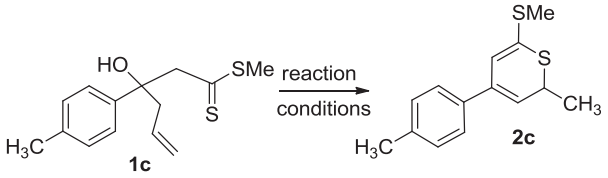
The synthetic utility of β-oxodithioesters has already been extensively explored by our group.[24] Consequently, as part of our continuing efforts to explore the chemical features of β-allylated derivatives of β-oxodithioesters, we hypothesized that β-allyl-β-hydroxy dithioester containing five reactive sites may undergo intramolecular heteroannulation to give thiopyran. So far, to the best of our knowledge, there is no report on the synthesis of thiopyrans from β-allyl-β-hydroxy dithioester through intramolecular dehydrative heteroannulation strategy. Therefore, we set out to explore the feasibility of β-allyl-β-hydroxy dithioesters **1** as reactive synthon to access thiopyrans **2** (Scheme 2).



Scheme 2. Synthesis of thiopyrans **2**.

We began our studies by using methyl 3-hydroxy-3-(*p*-tolyl) hex-5-enedithioate **1c** as test substrate. The solution of **1c** (1.0 mmol in 5 mL of dry chloroform) was treated with 1.0 equiv of $BF_3 \cdot Et_2O$ followed by stirring at room temperature for 15 h till the completion of the reaction (monitored by TLC). To our delight, work up of the reaction afforded the desired compound **2c** in 85% yield, characterized as 2-methyl-6-methylsulfanyl-4-*p*-tolyl-2*H*-thiopyran (Table 1, entry 1). Encouraged by the above result and further motivated by the importance of thiopyrans in natural products and medicinal chemistry, we set out to investigate this reaction in detail. To channel the reaction towards the formation of **2c**, we carried out a systematic survey of the reaction conditions by varying the catalysts, the solvent and the temperature. The results of various attempts are summarized in Table 1.

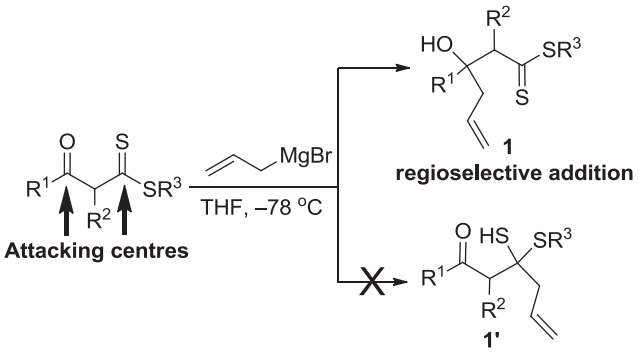
Table 1
Optimization of reaction conditions[a]



Entry	Catalyst	Loading (equiv)	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	$BF_3 \cdot Et_2O$	1.0	$CHCl_3$	rt	15	85
2	$BF_3 \cdot Et_2O$	1.0	$CHCl_3$	40	14	82
3	$BF_3 \cdot Et_2O$	1.0	$CHCl_3$	60	12	75
4	$BF_3 \cdot Et_2O$	1.0	DCE	rt	15	80
5	**$BF_3 \cdot Et_2O$**	**1.0**	**DCM**	**rt**	**15**	**92**
6	$BF_3 \cdot Et_2O$	1.0	CH_3CN	rt	48	—[c]
7	$BF_3 \cdot Et_2O$	1.0	THF	rt	48	—[c]
8	$InCl_3$	0.2	DCM	rt	48	—[c]
9	$Y(OTf)_3$	0.2	DCM	rt	48	—[c]
10	DMAP	0.2	DCM	rt	48	—[c]
11	DBU	0.2	DCM	rt	48	—[c]
12	Piperidine	0.2	DCM	rt	48	—[c]
13	$BF_3 \cdot Et_2O$	0.5	DCM	rt	15	71
14	$BF_3 \cdot Et_2O$	1.5	DCM	rt	15	84
15	—	—	DCM	rt	48	—[c]

The bold entry highlights the optimized condition.
[a] Reaction of adduct **1c** (1.0 mmol) under various conditions.
[b] Isolated pure yields.
[c] No formation of desired product.

The above model reaction was investigated at higher temperatures, and the results showed no improvement (Table 1, entries 2 and 3). To determine the ideal solvent for the transformation, we investigated the above reaction in various other solvents, such as dichloroethane (DCE), dichloromethane (DCM), CH_3CN and THF

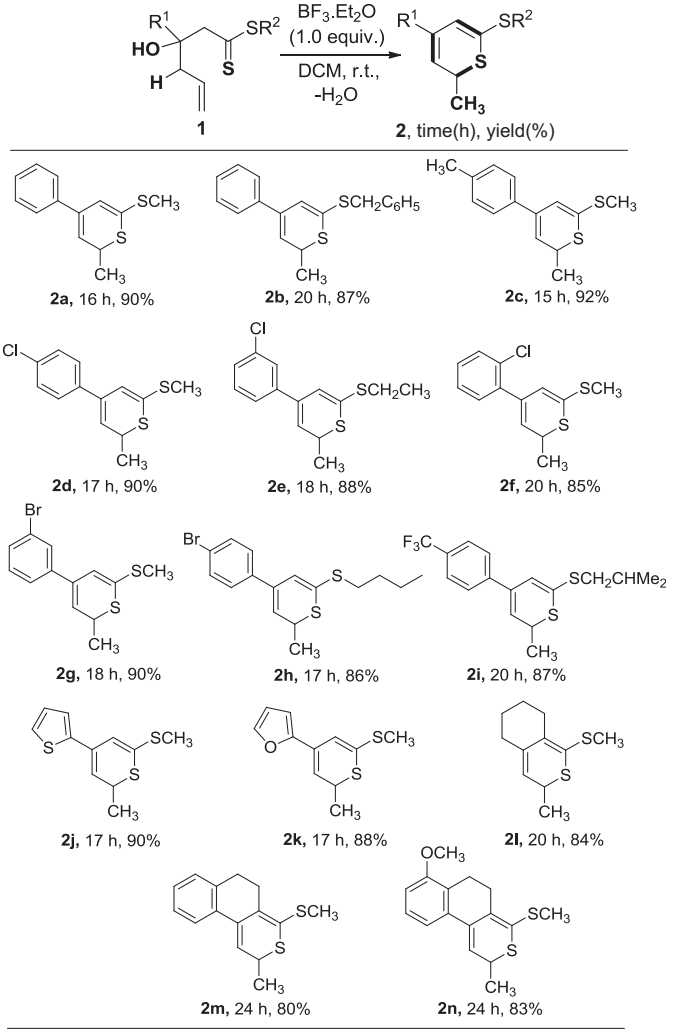


Scheme 1. Regioselective synthesis of **1**.

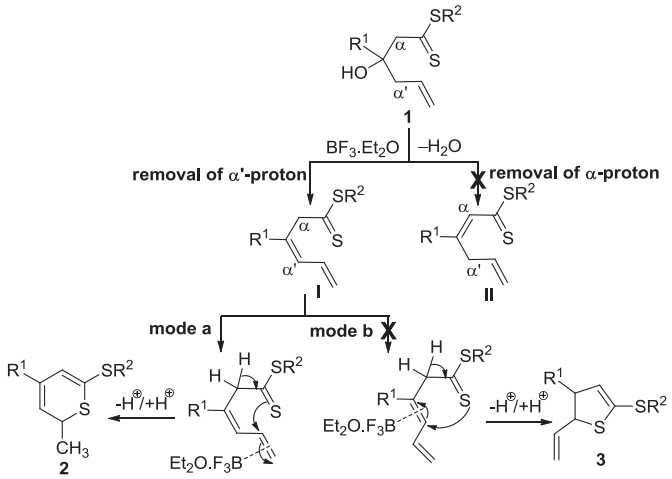
(Table 1, entries 4–7). DCM turned out to be an appropriate solvent affording the best isolated yield (92%) at room temperature. Next, other Lewis acids, such as $InCl_3$ and $Y(OTf)_3$, and bases like DMAP, DBU and piperidine were employed as the catalyst, but none of them could trigger the reaction to the desired direction (Table 1, entries 8–12). Next, we optimized the catalyst's loading, and it was found that either decreasing or increasing the catalyst's loading did not improve the result (Table 1, entries 13 and 14). Further, the blank reaction did not give the desired product in trace even after 48 h (Table 1, entry 15). Ultimately, optimal conditions were identified as 1.0 equiv of $BF_3\cdot Et_2O$ in DCM at room temperature (Table 1, entry 5).

Using the optimized reaction conditions, we evaluated the substrate scope of the reaction and the results are summarized in Table 2. As can be seen, a wide range of β-allyl-β-hydroxy dithioesters regardless of their electronic and steric nature were well-tolerated, and in all cases the reactions proceeded smoothly to afford the corresponding thiopyrans in good to excellent yields. Notably, β-allyl-β-hydroxy dithioesters **1** with either mono-substituted electron-donating or electron-withdrawing groups at various positions on the aryl ring of substituent R^1 showed almost similar reactivities and reacted efficiently to provide the desired thiopyrans **2a**–**i** in 85–92% yields. Even substrate **1** with R^1 as heteroaromatic substituents like 2-thienyl and 2-furyl took part in the reaction smoothly and afforded the corresponding thiopyrans **2j** and **2k** in 90% and 88% yields, respectively. Further, to broaden the scope of the reaction, β-allyl-β-hydroxy dithioesters derived from the dithioesters of cyclohexanone and α-tetralones were also employed in this protocol. To our pleasure, fused thiopyrans **2l**–**n** were obtained in 80–84% yields. These results further illustrate the generality and practical applicability of this novel strategy.

Table 2
Substrate scope for the synthesis of **2**

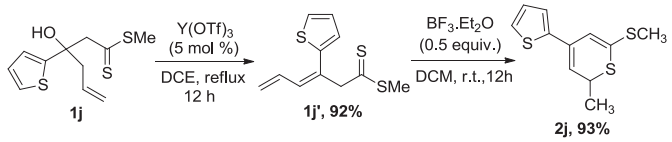


To rationalize the reaction outcomes, we proposed a tentative mechanism as shown in Scheme 3. The initial step includes the $BF_3\cdot Et_2O$ mediated regioselective dehydration to give the conjugated diene intermediate **I** by the removal of α′-proton of **1**.[25] Intermediate **I** may undergo cyclization by the attack of thiocarbonyl sulfur to the terminal and non-terminal double bonds activated by $BF_3\cdot Et_2O$ via two possible modes **a** and **b** to produce thiopyran **2** and dihydrothiophene **3**, respectively. Consequently, intermediate **I** undergoes regioselective attack of thiocarbonyl sulfur to its terminal double bond through mode **a** to give the desired thiopyran **2**. During our investigation we did not observe even a trace of **3**, and **2** was obtained exclusively. In the total course of the reaction $BF_3\cdot Et_2O$ plays a dual role by abstracting the OH for the removal of water (which probably cause the destruction of the catalyst to some extent) as well as activating the double bond and hence accounts for its use in equimolar ratio.



Scheme 3. Possible reaction mechanism.

To gain insight into the reaction mechanism, we treated our previously isolated diene product **1j′**[22] with $BF_3\cdot Et_2O$ in DCM at room temperature. To our delight, the diene has been quantitatively converted into our desired product **2j** within 12 h (observed by checking TLC pattern of the corresponding compounds) suggesting the intermediacy of **I** (Scheme 4).



Scheme 4. Experimental proof of the dehydration.

3. Conclusions

In summary, we have developed an operationally simple and straightforward protocol for the synthesis of 2*H*-thiopyrans through regioselective intramolecular annulation of β-allyl-β-hydroxy dithioesters mediated by $BF_3\cdot Et_2O$ at room temperature.

Reasonable mechanistic detail for the proposed intermediate involved in the annulation strategy is provided with experimental and literature evidences. We hope that the newly synthesized thiopyrans may act as precursors for further synthetic renovations to meet the need for diverse useful purposes. Overall, this clean and efficient protocol may be of value for both synthetic and medicinal chemists for academic research and practical applications.

4. Experimental section

4.1. General method

The commercially available allyl magnesium bromide and borontrifluoride diethyletherate ($BF_3{\cdot}Et_2O$) were used as received without any further purification. β-Oxodithioesters were prepared following the literature procedure.[26] Thin-layer chromatography (TLC) was performed using silica gel 60 F_{254} precoated plates. Column chromatography was performed with 100–200 mesh silica gel. 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 and 75.5 MHz, respectively. Chemical shifts (δ) are given in parts per million (ppm) using the residue solvent peaks as reference relative to TMS. Coupling constant (J) values are given in Hertz. Mass spectra were recorded using electrospray ionization (ESI) mass spectrometry. The melting points are uncorrected.

4.2. General procedure for the synthesis of 2-methyl-2*H*-thiopyrans (2a–n)

A solution of β-allyl-β-hydroxy dithioesters **1** (1.0 mmol) in dry dichloromethane (10 mL) was degassed for 15 min by continuous purging of ultrapure argon. Then $BF_3{\cdot}Et_2O$ (1.0 equiv) was added and the mixture was stirred at room temperature for the stipulated period of time. After completion of the reaction (monitored by TLC), 20 mL of water was added to the reaction mixture followed by extraction with chloroform (2×10 mL). The combined organic extract was dried over anhydrous Na_2SO_4 and then evaporated in vacuo. The crude residue thus obtained was purified by column chromatography over silica gel using increasing amounts of ethyl acetate in *n*-hexane as eluent to afford the pure 2-methyl-2*H*-thiopyrans **2**.

*4.2.1. 2-Methyl-6-methylsulfanyl-4-phenyl-2H-thiopyran (**2a**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.37–7.27 (m, 5H, Ar), 6.55 (s, 1H), 5.69 (d, J=6.0 Hz, 1H), 3.75–3.66 (m, 1H), 2.49 (s, 3H, SCH_3), 1.42 (d, J=6.9 Hz, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 140.2, 137.7, 134.5, 128.4, 127.5, 126.3, 119.7, 118.0, 36.7, 19.5, 18.0; IR (KBr, ν_{max}, cm^{-1}): 2965, 2922, 2857, 1494, 1445, 757, 698; MS: HRMS: m/z=234.0637 (M^+). Found: 234.0620 (M^+).

*4.2.2. 6-Benzylsulfanyl-2-methyl-4-phenyl-2H-thiopyran (**2b**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.36–7.22 (m, 10H, Ar), 6.62 (s, 1H), 5.69 (d, J=6.0 Hz, 1H), 4.13 (s, 2H, CH_2Ph), 3.66–3.62 (m, 1H), 1.36 (d, J=6.9 Hz, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 139.7, 137.6, 137.3, 132.0, 128.7, 128.3, 128.2, 127.4, 127.0, 126.1, 123.8, 118.6, 39.8, 36.7, 19.6; IR (KBr, ν_{max}, cm^{-1}): 2956, 2926, 2856, 1488, 1073, 1009, 800; MS: HRMS: m/z=310.0850 (M^+). Found: 311.0876 (M^++1).

*4.2.3. 2-Methyl-6-methylsulfanyl-4-p-tolyl-2H-thiopyran (**2c**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.25 (d, J=7.8 Hz, 2H, Ar), 7.13 (d, J=7.8 Hz, 2H, Ar), 6.54 (s, 1H), 5.66 (d, J=5.7 Hz, 1H), 3.74–3.65 (m, 1H), 2.49 (s, 3H, SCH_3), 2.34 (s, 3H, CH_3 attached to aryl ring), 1.41 (d, J=7.2 Hz, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 137.4, 137.3, 137.2, 134.3, 129.0, 126.1, 119.8, 117.3, 36.7, 21.0, 19.6, 17.9; IR (KBr, ν_{max}, cm^{-1}): 2920, 1513, 1446, 1019, 816, 796, 528.

*4.2.4. 4-(4-Chlorophenyl)-2-methyl-6-methylsulfanyl-2H-thiopyran (**2d**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.28 (br, 4H, Ar), 6.47 (s, 1H), 5.66 (d, J=6.0 Hz, 1H), 3.71–3.67 (m, 1H), 2.49 (s, 3H, SCH_3), 1.41 (d, J=6.9 Hz, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 138.6, 136.6, 135.3, 133.3, 128.5, 127.6, 119.0, 118.1, 36.6, 19.4, 17.9; IR (KBr, ν_{max}, cm^{-1}): 2923, 2853, 1491, 1092, 1013, 831, 799.

*4.2.5. 4-(3-Chlorophenyl)-6-ethylsulfanyl-2-methyl-2H-thiopyran (**2e**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.32 (s, 1H, Ar), 7.23 (d, J=2.7 Hz, 3H, Ar), 6.63 (s, 1H), 5.71 (d, J=5.7 Hz, 1H), 3.71–3.62 (m, 1H), 3.03–2.83 (m, 2H, CH_2 of SEt), 1.40 (d, J=6.9 Hz, 3H, Me), 1.31 (t, J=7.3 Hz, 3H, CH_3 of SEt); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 141.8, 136.6, 134.2, 133.4, 129.5, 127.4, 126.4, 124.4, 122.0, 119.0, 36.5, 29.2, 19.5, 14.7; IR (KBr, ν_{max}, cm^{-1}): 2969, 2925, 2867, 1475, 1447, 781, 694; MS: HRMS: m/z=282.0304 (M^+). Found: 283.0317 (M^++1).

*4.2.6. 4-(2-Chlorophenyl)-2-methyl-6-methylsulfanyl-2H-thiopyran (**2f**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.38–7.21 (m, 4H, Ar), 6.29 (s, 1H), 5.51 (d, J=5.7 Hz, 1H), 3.73–3.66 (m, 1H), 2.44 (s, 3H, SCH_3), 1.43 (d, J=6.9 Hz, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 139.7, 136.6, 132.7, 130.5, 129.7, 128.6, 126.6, 120.8, 120.1, 36.3, 19.6, 17.7; IR (KBr, ν_{max}, cm^{-1}): 2968, 2921, 2854, 1470, 1432, 1036, 757.

*4.2.7. 4-(3-Bromophenyl)-2-methyl-6-(methylthio)-2H-thiopyran (**2g**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.48 (d, J=12.0 Hz, 1H, Ar), 7.40 (d, J=7.8 Hz, 1H, Ar), 7.29–7.17 (m, 2H, Ar), 6.47 (s, 1H), 5.68 (d, J=5.7 Hz, 1H), 3.74–3.65 (m, 1H), 2.50 (s, 3H, SCH_3), 1.41 (d, J=7.2 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 142.5, 138.2, 130.5, 129.9, 129.5, 129.3, 125.0, 119.5, 119.2, 118.9, 36.7, 19.5, 18.0; IR (KBr, ν_{max}, cm^{-1}): 2961, 2922, 2854, 1473, 1072, 780, 693; MS: HRMS: m/z=311.9642 (M^+). Found: 312.9649 (M^++1).

*4.2.8. 4-(4-Bromophenyl)-6-butylsulfanyl-2-methyl-2H-thiopyran (**2h**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.42 (d, J=8.4 Hz, 2H, Ar), 7.20 (d, J=8.4 Hz, 2H, Ar), 6.62 (s, 1H), 5.69 (d, J=6.0 Hz, 1H), 3.70–3.61 (m, 1H), 2.99–2.81 (m, 2H, CH_2 of Bu), 1.66 (t, J=7.2 Hz, 2H, CH_2 of Bu), 1.41–1.39 (m, 5H, CH_3 and CH_2 of Bu), 0.89 (t, J=6.9 Hz, 3H, CH_3 of Bu); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 139.0, 136.8, 133.8, 131.4, 127.9, 121.9, 121.5, 118.4, 36.6, 35.0, 30.6, 22.2, 19.5, 13.9; IR (KBr, ν_{max}, cm^{-1}): 2962, 2923, 1445, 1371, 1128, 1016, 813, 748, 477; MS: HRMS: m/z=354.0212 (M^+). Found: 355.0229 (M^++1).

*4.2.9. 6-Isobutylsulfanyl-2-methyl-4-(4-trifluoromethyl-phenyl)-2H-thiopyran (**2i**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.58 (d, J=8.4 Hz, 2H, Ar), 7.45 (d, J=8.1 Hz, 2H, Ar), 6.65 (s, 1H), 5.76 (d, J=5.7 Hz, 1H), 3.72–3.67 (m, 1H), 2.91–2.75 (m, 2H, CH_2 of ^{i}Bu), 1.93–1.87 (m, 1H, CH of ^{i}Bu), 1.42 (d, J=6.9 Hz, 3H, Me), 1.03 (d, J=6.6 Hz, 6H, $2CH_3$ of ^{i}Bu); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 143.7, 136.9, 134.8, 129.7, 126.6, 125.4, 125.3, 121.4, 118.7, 43.9, 36.6, 28.9, 21.8, 21.7, 19.5; IR (KBr, ν_{max}, cm^{-1}): 2961, 2928, 1325, 1167, 1127, 1069; MS: HRMS: m/z=344.0880 (M^+). Found: 345.0899 (M^++1).

*4.2.10. 2-Methyl-6-methylsulfanyl-4-thiophen-2-yl-2H-thiopyran (**2j**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.16 (d, J=4.8 Hz, 1H, Ar), 7.05 (s, 1H, Ar), 6.97 (t, J=4.2 Hz, 1H, Ar), 6.58 (s, 1H), 5.81 (d, J=6.0 Hz, 1H), 3.73–3.64 (m, 1H), 2.50 (s, 3H, SCH_3), 1.41 (d, J=7.8 Hz, 3H, Me); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 135.5, 129.3, 127.4, 125.6, 124.1, 123.0, 118.4, 116.4, 36.6, 19.4, 17.9.

*4.2.11. 2-Methyl-6-methylsulfanyl-4-furan-2-yl-2H-thiopyran (**2k**).* Beige oil. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.35 (br, 1H, Ar),

6.54 (br, 1H), 6.36 (d, J=9.3 Hz, 2H), 5.96 (d, J=2.4 Hz, 1H), 3.72–3.68 (m, 1H), 2.49 (s, 3H, SMe), 1.41 (d, J=3.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 141.8, 140.4, 134.4, 120.0, 116.4, 114.9, 111.1, 105.3, 36.1, 19.6, 17.9.

*4.2.12. 3-Methyl-1-(methylthio)-5,6,7,8-tetrahydro-3H-isothio chromene (**2l**).* Beige coloured viscous liquid. (Diastereomeric mixture) ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 5.96 (d, J=6.0 Hz, 1H), 3.72–3.68 (m, 1H), 2.49 (s, 3H, SMe), 2.17 (br, 8H), 1.41 (d, J=3.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 137.2, (131.6, 131.1), (126.8, 126.7), 122.3, 41.2, 37.0, 28.5, 25.9, (23.2, 22.6), (20.0, 19.9), (17.3, 17.2).

*4.2.13. 2-Methyl-4-(methylthio)-5,6-dihydro-2H-benzo[f]isothio chromene (**2m**).* Beige coloured viscous liquid. (Diastereomeric mixture) ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.52 (t, J=2.7 Hz, 1H, Ar), 7.24–7.12 (m, 3H, Ar), 6.99 (d, J=5.7 Hz, 1H), 3.62–3.57 (m, 1H), 2.87–2.68 (m, 4H), 2.45 (s, 3H, SMe), 1.39 (dd, J=3.0, 1.5 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 137.4, 134.8, 134.7, 132.1, (127.7, 127.5), (127.1, 127.0), (126.6, 126.4), 124.2, (123.6, 123.5), (118.4, 118.1), (35.1, 34.9), 29.6, 27.2, (19.7, 19.6), (19.0, 18.8); HRMS: m/z=260.0693 (M^+). Found: 260.0641 (M^+).

*4.2.14. 7-Methoxy-2-methyl-4-(methylthio)-5,6-dihydro-2H-benzo [f]isothiochromene (**2n**).* Beige coloured viscous liquid. (Diastereomeric mixture) ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.24–7.11 (m, 2H, Ar), 6.74 (d, J=6.0 Hz, 1H, Ar), 6.00 (d, J=6.0 Hz, 1H), 3.82 (s, 3H, OMe), 3.61–3.54 (m, 1H), 2.88–2.66 (m, 4H), 2.44 (s, 3H, SMe), 1.39 (d, J=3.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm): 156.1, 135.9, 134.7, 132.4, 126.6, 126.2, 123.9, (118.6, 118.5), 116.1, 108.8, (55.5, 55.4), 35.1, 26.7, 21.5, 19.6, 19.0.

Acknowledgements

We gratefully acknowledge the generous financial support from SERB, the Department of Science and Technology (Grant No. SR/S1/OC-66/2009), the Council of Scientific and Industrial Research (Grant No. 02(0072)/12/EMR-II), and the UGC-UKIERI Partnership-2013 (Grant No. 184-16/2013(IC), New Delhi). We are thankful to Prof. Ganesh Pandey, CBMR, SGPGI, Lucknow and Prof. Manas Ghorai, IIT Kanpur for their help in recording of HRMS spectra.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.12.020.

References and notes

1. (a) Ingall, A. H. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, U.K., 1984; Vol. 3, p 885; and references therein; (b) Mayer, R.; Broy, W.; Zahradnik, R. *Adv. Heterocycl. Chem.* **1967**, *8*, 219 and references therein; (c) Hepworth, J. D.; Gabbutt, C. D.; Heron, B. M. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, U.K., 1996; Vol. 5, p 325; (d) Tavakolinia, F.; Baghipour, T.; Hossaini, Z.; Zareyee, D.; Khalilzadeh, M. A.; Rajabi, M. *Nucleic Acid Ther.* **2012**, *22*, 265; (e) Schneller, W. *Adv. Heterocycl. Chem.* **1975**, *18*, 59.
2. (a) Lawson, K. R.; McDonald, B. P.; Mills, O. S.; Steele, R. W.; Sutherland, J. K.; Wear, T. J.; Brewster, A.; Marsham, P. R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 663; (b) Nair, S. K.; Jose, A. M.; Asokan, C. V. *Synthesis* **2005**, 1261; (c) Vedeje, E.; Krafft, G. A. *Tetrahedron* **1982**, *38*, 2857.
3. (a) Sun, X.; Wong, J. R.; Song, K.; Hu, J.; Garlid, K. D.; Chen, L. B. *Cancer Res.* **1994**, *54*, 1465; (b) Bertenshaw, D. E.; Getman, D.; Heintz, R. M.; Talley, J. J.; Reed, K. L.; Chruschiel, R. A.; Clare, M. PCT Int. Appl. WO 9414793 A1 19940707, 1994; *Chem. Abstr.* **1994**, *123*, 169509. (c) Britton, J. E.; Fang, J.; Heyer, D.; Miller, A. B.; Navas, F., III; Smalley, T. L., Jr.; Zuercher, W. J.; Kalamreddy, S. R. PCT Int. Appl. WO 2005012220 A2 20050210, 2005; *Chem. Abstr.* **2005**, *142*, 219151. (d) Daniel, D.; Rene, R. *Eur. J. Med. Chem.* **1984**, *19*, 477; (e) Sawaki, M.; Iwataki, I.; Hirono, Y.; Ishikawa, H.; Wakai, A.; Asada, M. Japanese Patent 75129565, 1978; *Chem. Abstr.* **1978**, *89*, 43112. (f) Herrinton, P. M.; Owen, C. E.; Gage, J. R. *Org. Process Res. Dev.* **2001**, *5*, 80.
4. (a) Casy, G.; Taylor, R. J. K. *Tetrahedron* **1989**, *45*, 455; (b) Casy, G.; Taylor, R. J. K. *J. Chem. Soc., Chem. Commun.* **1988**, 454.
5. Ward, D. E.; Jheengut, V.; Beye, G. E. *J. Org. Chem.* **2006**, *71*, 8989.
6. (a) McDonald, B. P.; Steele, R. W.; Sutherland, J. K.; Leslie, B. W.; Brewster, A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 675; (b) Casy, G.; Lane, S.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1397.
7. McAllister, G. D.; Taylor, R. J. K. *Tetrahedron Lett.* **2001**, *42*, 1197.
8. Brown, M. J.; Carter, P. S.; Fenwick, A. S.; Fosberry, A. P.; Hamprecht, D. W.; Hibbs, M. J.; Jarvest, R. L.; Mensah, L.; Milner, P. H.; O'Hanlon, P. J.; Pope, A. J.; Richardson, C. M.; West, A.; Witty, D. R. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3171.
9. Quaglia, W.; Pigini, M.; Piergentili, A.; Giannella, M.; Gentili, F.; Marucci, G.; Carrieri, A.; Carotti, A.; Poggesi, E.; Leonardi, A.; Melchiorre, C. J. *J. Med. Chem.* **2002**, *45*, 1633.
10. Van Vliet, L. A.; Rodenhuis, N.; Dijkstra, D.; Wikstrom, H.; Pugsley, T. A.; Serpa, K. A.; Meltzer, L. T.; Heffner, T. G.; Wise, L. D.; Lajiness, M. E.; Huff, R. M.; Svensson, K.; Sundell, S.; Lundmark, M. *J. Med. Chem.* **2000**, *43*, 2871.
11. Wang, W.; Li, H.; Wang, J.; Zu, L. S. *J. Am. Chem. Soc.* **2006**, *128*, 10354.
12. Sugita, Y.; Hosoya, H.; Terasawa, K.; Yokoe, I.; Fijisawa, S.; Sakagami, H. *Anticancer Res.* **2001**, *21*, 2629.
13. Hollick, J. J.; Golding, B. T.; Hardcastle, I. R.; Martin, N.; Richardson, C.; Rigoreau, L. J.; Smith, G. C.; Griffin, R. J. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3083.
14. (a) Saito, T.; Takekawa, K.; Takahashi, T. *Chem. Commun.* **1999**, 1001; (b) Barnish, I. T.; Fishwick, C. W. G.; Hill, D. R.; Szantay, C., Jr. *Tetrahedron* **1989**, *45*, 7879; (c) Bell, A. S.; Fishwick, C. W. G.; Reed, J. E. *Tetrahedron* **1998**, *54*, 3219; (d) Dentel, H.; Chataigner, I.; Le Cavelier, F.; Gulea, M. *Tetrahedron Lett.* **2010**, *51*, 6014; (e) Riu, A.; Harrison-Marchand, A.; Maddaluno, J.; Gulea, M.; Albadri, H.; Masson, S. *Eur. J. Org. Chem.* **2007**, 4948.
15. Jagodzinski, T. S.; Sosnicki, J. G.; Wesolowska, A. *Tetrahedron* **2003**, *59*, 4183.
16. Bondalapati, S.; Gogoi, P.; Indukuri, K.; Saikia, A. K. *J. Org. Chem.* **2012**, *77*, 2508.
17. Spagnol, G.; Heck, M.-P.; Nolan, S. P.; Mioskowski, C. *Org. Lett.* **2002**, *4*, 1767.
18. (a) Barthakur, M. G.; Chetia, A.; Boruah, R. C. *Tetrahedron Lett.* **2006**, *47*, 4925; (b) Rostami-Charati, F. *Synlett* **2013**, 2137.
19. (a) Padwa, A.; Gareau, Y.; Harrison, B.; Rodriguez, A. *J. Org. Chem.* **1992**, *57*, 3540; (b) Verma, R. K.; Verma, G. K.; Shukla, G.; Nagaraju, A.; Singh, M. S. *ACS Comb. Sci.* **2012**, *14*, 224; (c) Koley, S.; Chowdhury, S.; Chanda, T.; Ramulu, B. J.; Singh, M. S. *Tetrahedron* **2013**, *69*, 8013.
20. Kenny, R. S.; Mashelkar, U. C.; Rane, D. M.; Bezawada, D. K. *Tetrahedron* **2006**, *62*, 9280.
21. Gabbutt, C. D.; Hepworth, J. D.; Heron, B. M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2603.
22. Chowdhury, S.; Chanda, T.; Nandi, G. C.; Koley, S.; Ramulu, B. J.; Pandey, S. K.; Singh, M. S. *Tetrahedron* **2013**, *69*, 8899.
23. Masson, S.; Thuillier, A. *Tetrahedron Lett.* **1982**, *23*, 4087.
24. Recent papers on dithioesters: (a) Nandi, G. C.; Samai, S.; Singh, M. S. *J. Org. Chem.* **2010**, *75*, 7785; (b) Nandi, G. C.; Samai, S.; Singh, M. S. *J. Org. Chem.* **2011**, *76*, 8009; (c) Chowdhury, S.; Nandi, G. C.; Samai, S.; Singh, M. S. *Org. Lett.* **2011**, *13*, 3762; (d) Nandi, G. C.; Singh, M. S.; Ila, H.; Junjappa, H. *Eur. J. Org. Chem.* **2012**, 967; (e) Verma, R. K.; Verma, G. K.; Raghuvanshi, K.; Singh, M. S. *Tetrahedron* **2011**, *67*, 584; (f) Verma, G. K.; Verma, R. K.; Singh, M. S. *RSC Adv.* **2013**, *3*, 245; (g) Singh, M. S.; Nagaraju, A.; Verma, G. K.; Shukla, G.; Verma, R. K.; Srivastava, A.; Raghuvanshi, K. *Green Chem.* **2013**, *15*, 954; (h) Ramulu, B. J.; Chanda, T.; Chowdhury, S.; Nandi, G. C.; Singh, M. S. *RSC Adv.* **2013**, *3*, 5345; (i) Chowdhury, S.; Chanda, T.; Koley, S.; Ramulu, B. J.; Jones, R. C. F.; Singh, M. S. *Org. Lett.* **2013**, *15*, 5386.
25. (a) Wang, L.; Xie, X.; Liu, Y. *Org. Lett.* **2012**, *14*, 5848; (b) Yin, G.; Zhu, Y.; Lu, P.; Wang, Y. *J. Org. Chem.* **2011**, *76*, 8922; (c) Yin, G.; Zhu, Y.; Zhang, L.; Lu, P.; Wang, Y. *Org. Lett.* **2011**, *13*, 940.
26. Samuel, R.; Asokan, C. V.; Suma, S.; Chandran, P.; Retnamma, S.; Anabha, E. R. *Tetrahedron Lett.* **2007**, *48*, 8376.