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Regioselective synthesis of pentacyclic heterocycles by sequential [3,3] sigmatropic rearrangement of 2-(4′-aryloxybut-2′-ynyl-mercapto)thiochromen-4-ones

K. C. Majumdar,* A. Bandyopadhyay and A. Biswas

Department of Chemistry, University of Kalyani, Kalyani 741 235, W.B., India

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Abstract—A number of 4-aryloxymethyl-7-chlorothiopyrano[2,3-*b*]thiochromen-5(2*H*)-ones are regioselectively synthesized in 80–85% yield by the Claisen rearrangement of 2-(4′-aryloxybut-2′-ynylmercapto)thiochromen-4-ones in refluxing chlorobenzene for 3 h. These products are then subjected to a second Claisen rearrangement in refluxing *N*,*N*-diethylaniline for 6 h to give hitherto unreported pentacyclic heterocycles in 50–55% yield.

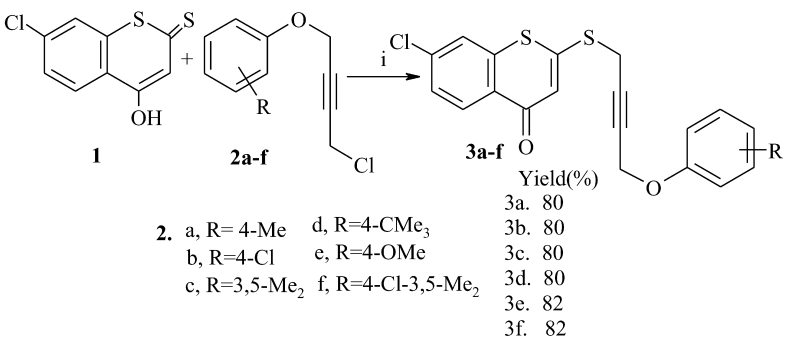
1. Introduction

Our continued interest in the synthesis of different oxygen,[1] nitrogen[2] and sulfur[3] heterocycles by the application of sigmatropic rearrangements[4] led us to synthesize a number of hitherto unreported heterocyclic compounds derived from 4-hydroxydithiocoumarin.[5,6] This also included a simple synthesis of the thieno[2,3-*b*]thiochromen-4-one skeleton, an intermediate for the synthesis of a number of drugs[7] used for psycotic disturbances. Earlier we reported the sequential [3,3] sigmatropic rearrangements of suitably 1,4-disubstituted but-2-ynes to give interesting results[8–10] and this has prompted us to take a study on the sequential [3,3] sigmatropic rearrangements of 2-(4′-aryloxybut-2′-ynylmercapto)thiochromen-4-ones. Here we report the results.

2. Results and discussion

2-(4′-Aryloxybut-2′-ynylmercapto)-7-chlorothiochromen-4-ones were prepared in 80–82% yield by the phase transfer catalyzed alkylation[11] of 7-chloro-4-hydroxydithiocoumarin[6] **1** with a number of 1-aryloxy-4-chlorobut-2-yne **2a–f** in the presence of benzyltriethylammonium-chloride (BTEAC) in 1% aqueous NaOH–$CHCl_3$ for 5 h. The same reaction if conducted under classical conditions of refluxing in acetone in the presence of anhydrous potassium carbonate for 6–8 h afforded the substrates **3a–f** in lower yields (55–70%) (Scheme 1).

The substrates **3a–f** contain the but-2-ynylthioenone moiety as well as the arylprop-2-ynylether moiety and thus offers scope for two different possibilities of [3,3] sigmatropic



Scheme 1. *Reagents and conditions*: (i) BTEAC, aq. NaOH (1%), $CHCl_3$, 5 h.

Keywords: [3,3] sigmatropic rearrangement; regioselective synthesis; sequential Claisen rearrangement; phase-transfer catalysis.

* Corresponding author. Tel.: +91-33-2582-7521; fax: +91-33-25828282; e-mail: kcm@klyuniv.ernet.in

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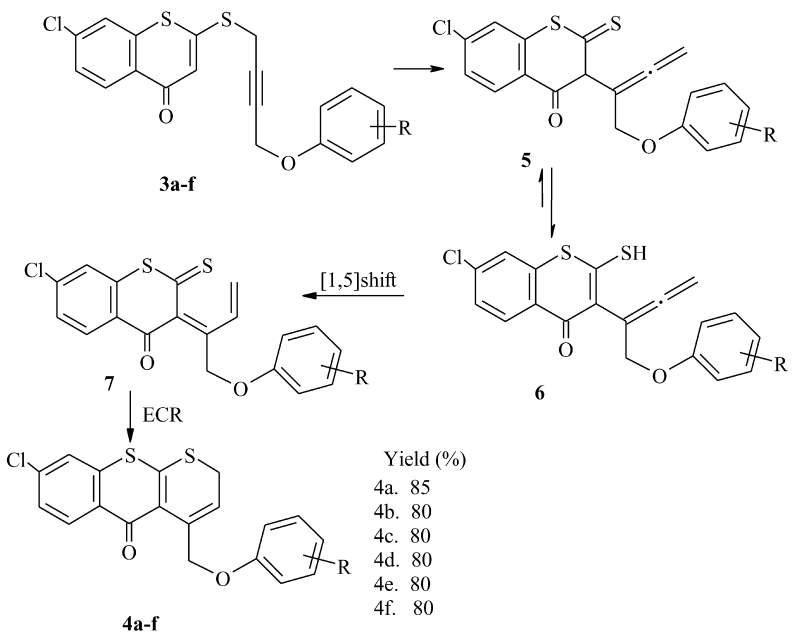


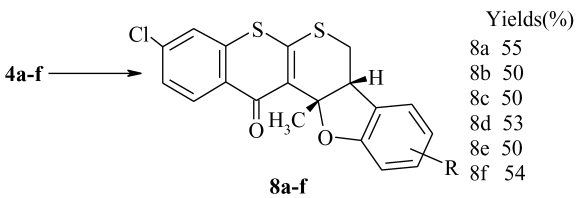
Scheme 2. *Reagents and conditions*: C_6H_5Cl, 3 h, reflux.

rearrangement. The aliphatic Claisen rearrangement has lower activation energy as the aromatic counterpart has its aromatic sextet disturbed in the transition state. Therefore, substrate **3a** was heated in chlorobenzene (132°C) and the reaction was monitored by TLC. Complete conversion was achieved in 3 h giving a white solid, mp 102°C, isolated in 80% yield. The product **4a** was characterized from its elemental analysis and spectroscopic data as 7-chloro-4-(4′-methylphenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5(2*H*)-one. Substrates **3b**–**f** under similar treatment gave products **4b**–**f** in 80–85% yields (Scheme 2). The formation of products **4a**–**f** from substrates **3a**–**f** may be easily explained by an initial [3,3] sigmatropic rearrangement followed by rapid enolization to give intermediate allenyl thiol **6**, [1,5] hydrogen shift and 6π-electrocyclic ring closure may finally give products **4a**–**f** (Scheme 2).

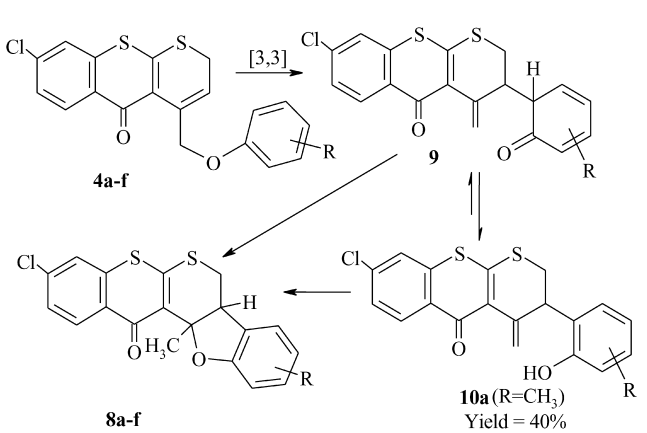
A close examination of products **4a**–**f** reveals that these still contain an allyl aryl ether moiety well situated for a second Claisen rearrangement. Substrate **4a** was heated in 1,2-dichlorobenzene in the presence of a catalytic amount of aniline and after 14 h, a new compound was obtained. This was characterized as **10** (Scheme 4) from its elemental analysis and spectroscopic data. Its ^{1}H NMR spectrum revealed-δ 2.17 (s, 3H, CH_3), 3.30–3.64 (m, 2H, SCH_2), 4.34–4.36 (m, 1H, allylic *H*), 5.19 (s, 1H, one exocyclic *H*), 6.08 (s, 1H, one exocyclic *H*), 6.60–6.72 (m, 5H, Ar*H*), 8.36–8.39 (d, 1H, *J*=8.5 Hz, Ar*H*). This compound was subjected to cyclization by (i) pyridine hydrotribromide, (ii) hexamine hydrotribromide, (iii) H_2SO_4. The compound showed a tendency to decomposition and no tractable product was obtained. Substrate **4a** was next heated in refluxing *N*,*N*-diethylaniline for 6 h to give a crystalline solid, mp 145°C (50%). This was characterized as **8a** (Scheme 3) from its elemental analysis and spectral data. Its ^{1}H NMR spectrum showed δ 1.78 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.83–2.91 (dd, 1H, *J*=12.0, 13.0 Hz, SCH_2), 2.98–3.04 (dd, 1H, *J*=4.0, 13.0 Hz, SCH_2), 3.46–3.52 (dd, 1H, *J*=4.0, 12.0 Hz, 1H of ring junction), 6.85–7.42 (m, 5H, Ar*H*); 8.42 (d, 1H, *J*=8.5 Hz, Ar*H*). Substrates **4b**–**f** were also similarly treated to give products **8b**–**f**. The stereochemistry of the furothiopyran ring juncture of **8** can only be surmised from the molecular model (Dreiding model) of the molecules which show a strain free *cis* arrangement (Scheme 3).

The formation of products **8a**–**f** can be mechanistically explained by an initial [3,3] sigmatropic rearrangement in **4a**–**f** to give dienone **9**, enolization converts **9** into **10** which may then undergo a 5-exo cyclization to give **8** (Scheme 4).

In conclusion, we have executed the sequential Claisen



Scheme 3. *Reagents and conditions*: *N*,*N*-diethylaniline, reflux, 6 h.



Scheme 4.

rearrangement, at the present instance a *thio*-Claisen rearrangement of propynyl vinyl sulfide followed by an *oxy*-Claisen rearrangement of allyl phenyl ether. This methodology represents a straight forward approach for the construction of the furothiopyran ring system. This has been applied for the synthesis of pentacyclic heterocycles from 2-(4′-aryloxybut-2′-enylmercapto)thiochromen-4-ones.

3. Experimental

Melting points are uncorrected. UV absorption spectra were recorded on a UV–VIS Spectrophotometer Shimadzu Model No. UV-2401PC (absolute ethanol). IR spectra were run as KBr discs on a Perkin–Elmer 1330 apparatus and FTIR spectrophotometer Perkin–Elmer Model No.L120-000A. ^{1}H NMR spectra were recorded in $CDCl_3$ with TMS as internal standard on a Bruker DPX-300 (300 MHz) and Bruker DRS-600 (500 MHz) spectrometers. Elemental analyses and mass spectras were recorded on a [JEOL D-300 (El)] instrument by RSIC(CDRI) Lucknow. Silica gel (60–120) was obtained from Spectrochem. Extracts were dried over anhydrous Na_2SO_4.

3.1. Alkylation of 7-chloro-4-hydroxydithiocoumarin

To a mixture of 7-chloro-4-hydroxydithiocoumarin (6 mmol) and 1-aryloxy-4-chlorobut-2-yne (9 mmol) in chloroform (50 mL) is added a solution of TBAB (0.25 mmol) or (BTEAC) (0.9 mmol) in 1% aq. NaOH (50 mL) and the mixture was stirred at room temperature for a period of 5 h. The mixture was then diluted with water (100 mL) and extracted with $CHCl_3$ (3×25 mL), brine (3×25 mL) and dried (Na_2SO_4). The solvent was removed in vacuo and the residual crude mass was purified by chromatography over silica gel using benzene–petroleum ether (1:2) as eluent to afford the following compounds.

3.1.1. 7-Chloro-2-[4-(4′-methylphenoxybut-2′-ynylthio)][1]benzothiopyran-4-one (3a). White solid, mp 95°C; yield 80% (1.85 g); UV (EtOH) λ_{max}: 219 (log ε=4.25), 272 (log ε=4.50), 336 (log ε=4.16) nm; IR (KBr) ν_{max}: 1600, 1580, 1230 cm^{-1}; ^{1}H NMR (300 MHz): δ 2.27 (s, 3H, $-CH_3$); 3.67 (t, 2H, J=2.0 Hz, $-SCH_2$), 4.62 (t, 2H, J=2.0 Hz, $-OCH_2$), 6.76–7.95 (m, 7H, Ar*H*); 8.37 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m*/*z*: 388 (3.2), 386 (12.4, M$^+$), 279 (31.2), 122 (100), 121 (61.2), 107 (100), 91 (31.2%). Anal. Calcd for $C_{20}H_{15}ClO_2S_2$: C, 62.18; H, 3.89%. Found C, 62.07; H, 3.94%.

3.1.2. 7-Chloro-2-[4-(4′-chlorophenoxybut-2′-ynylthio)][1]benzothiopyran-4-one (3b). White solid, mp 102°C; yield 80% (2.0 g); UV (EtOH) λ_{max}: 221 (log ε=4.24), 271 (log ε=4.43), 343 (log ε=4.15) nm; IR (KBr) ν_{max}: 1600, 1580, 1260 cm^{-1}; ^{1}H NMR (300 MHz): δ 3.85 (t, 2H. J=2.0 Hz, $-SCH_2$), 4.81 (t, 2H, J=2.0 Hz, $-OCH_2$), 6.82–7.51 (m, 7H, Ar*H*); 8.42 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m*/*z*:410 (2.4), 408 (4.6) 406 (6.8, M$^+$), 279 (22.8), 128 (100), 127 (58.1), 109 (100), 91 (28.7%). Anal. calcd for $C_{19}H_{12}Cl_2O_2S_2$: C, 56.01; H, 2.94%. Found C, 56.06; H, 2.98%.

3.1.3. 7-Chloro-2-[4-(3′,5′-dimethylphenoxybut-2′-ynylthio)][1]benzothiopyran-4-one (3c). White solid, mp 103°C; yield 80% (1.92 g); UV (EtOH) λ_{max}: 219 (log ε=4.26), 271 (log ε=4.48), 337 (log ε=4.18) nm; IR (KBr) ν_{max}: 1600, 1580, 1290 cm^{-1}; ^{1}H NMR (500 MHz): δ 2.23 (s, 6H, $2CH_3$); 3.83 (t, 2H. J=2.0 Hz, $-SCH_2$), 4.66 (t, 2H, J=2.0 Hz, $-OCH_2$), 6.53–7.47 (m, 6H, Ar*H*); 8.38 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m*/*z*: 402 (2.1), 400 (14.9, M$^+$), 279 (34), 173 (92.55), 172 (72.3), 122 (100), 121 (58.5), 107 (100), 91 (34%). Anal. calcd for $C_{21}H_{17}ClO_2S_2$: C, 63.00; H, 4.25%. Found C, 63.21; H, 4.19%.

3.1.4. 7-Chloro-2-[4-(4′-tert.butylphenoxybut-2′-ynylthio)][1]benzothiopyran-4-one (3d). White solid, mp 58°C; yield 80% (2.0 g); UV (EtOH) λ_{max}: 217 (log ε=4.25), 270 (log ε=4.49), 336 (log ε=4.15) nm; IR (KBr) ν_{max}: 1622, 1584, 1306 cm^{-1}; ^{1}H NMR (300 MHz): δ 1.27 (s, 9H, $C(CH_3)_3$); 3.84 (t, 2H. J=2.0 Hz, $-SCH_2$), 4.67 (t, 2H, J=2.0 Hz, $-OCH_2$), 6.83–7.49 (m, 7H, Ar*H*); 8.38 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m*/*z*: 430 (3.2), 428 (6.4, M$^+$), 413 (5.1), 279 (27.7), 150 (100), 136 (87.2), 135 (100), 107 (100), 95 (79.8), 91 (60.6%). Anal. calcd for $C_{23}H_{21}ClO_2S_2$: C, 64.41; H, 4.90%. Found C, 64.60; H, 4.65%.

3.1.5. 7-Chloro-2-[4-(4′-methoxyphenoxybut-2′-ynylthio)][1]benzothiopyran-4-one (3e). White solid, mp 92°C; yield 82% (1.98 g); UV (EtOH) λ_{max}: 218 (log ε=4.24), 271 (log ε=4.43), 336 (log ε=4.14) nm; IR (KBr) ν_{max}: 1600, 1582, 1270 cm^{-1}; ^{1}H NMR (300 MHz): δ 3.72 (s, 3H, $-OCH_3$), 3.83 (t, 2H, J=2.0 Hz, $-SCH_2$), 4.64 (t, 2H, J=2.0 Hz, $-OCH_2$), 6.73–7.48 (m, 7H, Ar*H*), 8.39 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m*/*z*: 404 (5.3), 402 (10.6, M$^+$), 279 (22.3), 124 (100), 123 (62.7), 109 (100), 95 (22.3%). Anal. calcd for $C_{20}H_{15}ClO_3S_2$: C, 59.62; H, 3.72%. Found C, 59.70; H, 3.60%.

3.1.6. 7-Chloro-2-[4-(4′-chloro-3′,5′-dimethylphenoxybut-2′-ynylthio)][1]benzothiopyran-4-one (3f). White solid, mp 120°C; yield 82% (2.15 g); UV (EtOH) λ_{max}: 212 (log ε=4.25), 261 (log ε=4.46), 340 (log ε=4.18) nm; IR (KBr) ν_{max}: 1600, 1582, 1270 cm^{-1}; ^{1}H NMR (300 MHz): δ 2.28 (s, 6H, $2CH_3$), 3.83 (t, 2H, J=2.0 Hz, $-SCH_2$), 4.64 (t, 2H, J=2.0 Hz, $-OCH_2$), 6.62–7.48 (m, 5H, Ar*H*), 8.37 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m*/*z*: 438 (1.6), 436 (4.4), 434 (5.3, M$^+$), 279 (15.9), 256 (60.2), 156 (100), 129 (45.7), 121 (100), 97 (71.3), 91 (94.7%). Anal. calcd for $C_{21}H_{16}Cl_2O_2S_2$: C, 57.93; H, 3.67%. Found C, 57.90; H, 3.63%.

3.2. General procedure for rearrangement of compound 3a–f

The starting sulfide (0.5 g, 1.25 mmol) was refluxed in chlorobenzene (4 mL) in an oil bath for 2 h. Chlorobenzene was removed in vacuo and the residual mass was chromatographed over silica gel. Elution of the column with pet-ether (60–80°C) removed the residual chlorobenzene and then white solid was obtained by eluting the column with benzene–petether (60–80°C) 1:1.

3.2.1. 8-Chloro-4-(4′-methylphenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5-(2*H*)-one (4a). White solid,

mp 100°C; yield 85% (410 mg); UV (EtOH) λ_{max}: 240 (log ε=4.22), 295 (log ε=4.52), 336 (log ε=3.93) nm; IR (KBr) ν_{max}: 1620, 1580, 1380 cm^{-1}; ^1H NMR (500 MHz): δ 2.25 (s, 3H, $-CH_3$); 3.42 (d, 2H. J=6.0 Hz, $-SCH_2$), 5.50 (s, 2H, $-OCH_2$), 6.15–6.17–7.47 (m, 7H, Ar*H*); 8.28 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 388 (4.3), 386 (8.5, M^+), 281 (100), 280 (58.5), 279 (100), 216 (14.9), 171 (21.3), 107 (77.6), 91 (17%). Anal. calcd for $C_{20}H_{15}ClO_2S_2$: C, 62.18; H, 3.89%. Found C, 62.02; H, 3.90%.

3.2.2. 8-Chloro-4-(4′-chlorophenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5-(2*H*)-one (4b). White solid, mp 99°C; yield 80% (407 mg); UV (EtOH) λ_{max}: 242 (log ε=4.21), 298 (log ε=4.49), 355 (log ε=3.96) nm; IR (KBr) ν_{max}: 1620, 1600, 1490 cm^{-1}; ^1H NMR (500 MHz): δ 3.42 (d, 2H. J=6.0 Hz, $-SCH_2$), 5.06 (s, 2H, $-OCH_2$), 6.13–7.47 (m, 7H, Ar*H*); 8.28 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*:410 (1.4), 408 (4.6), 406 (2.4, M^+), 281 (52.3), 280 (34.5), 279 (100), 121 (36.8), 107 (23.4), 91 (25.6%). Anal. calcd for $C_{19}H_{12}Cl_2O_2S_2$: C, 56.01; H, 2.94%. Found C, 56.08; H, 3.01%.

3.2.3. 8-Chloro-4-(3′,5′-dimethylphenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5-(2*H*)-one (4c). White solid, mp 138°C; yield 80% (402 mg); UV (EtOH) λ_{max}: 220 (log ε=4.21), 292 (log ε=4.52), 351 (log ε=3.97) nm; IR (KBr) ν_{max}: 1613, 1582, 1378 cm^{-1}; ^1H NMR (300 MHz): δ 2.25 (s, 6H, $2CH_3$); 3.42 (d, 2H. J=6.0 Hz, $-SCH_2$), 5.04 (s, 2H, $-OCH_2$), 6.15–7.47 (m, 6H, Ar*H*); 8.29 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 402 (2.1), 400 (4.3, M^+), 281 (100), 280 (76.59), 279 (100), 216 (18.1), 171 (12.8), 122 (21.3), 107 (21.3), 91 (18.1%). Anal. calcd for $C_{21}H_{17}ClO_2S_2$: C, 63.00; H, 4.25%. Found C, 62.19; H, 4.31%.

3.2.4. 8-Chloro-4-(4′-tert.butylphenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5-(2*H*)-one (4d). White solid, mp 74°C; yield 80% (427 mg); UV (EtOH) λ_{max}: 221 (log ε=4.18), 291 (log ε=4.48), 343 (log ε=3.91) nm; IR (KBr) ν_{max}: 1617, 1582, 1383 cm^{-1}; ^1H NMR (300 MHz): δ 1.27 (s, 9H, $C(CH_3)_3$); 3.42 (d, 2H. J=6.0 Hz, $-SCH_2$), 5.05 (s, 2H, $-OCH_2$), 6.15–7.46 (m, 7H, Ar*H*); 8.28 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 430 (1.8), 428 (4.5, M^+), 281 (100), 280 (75.9), 279 (100), 252 (39.4), 224 (26.6), 150 (37.2), 135 (100), 107 (68.1), 91 (28.7%). Anal. calcd for $C_{23}H_{21}ClO_2S_2$: C, 64.41; H, 4.90%. Found C, 64.25; H, 4.78%.

3.2.5. 8-Chloro-4-(4′-methoxylphenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5-(2*H*)-one (4e). White solid, mp 102°C; yield 80% (404 mg); UV (EtOH) λ_{max}: 223 (log ε=4.20), 292 (log ε=4.51), 353 (log ε=3.96) nm; IR (KBr) ν_{max}: 1610, 1586, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 3.42 (d, 2H. J=6.0 Hz, $-SCH_2$), 3.74 (s, 3H, $-OCH_3$), 5.03 (s, 2H, $-OCH_2$), 6.14–7.47 (m, 6H, Ar*H*); 8.28 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 404 (3.8), 402 (9, M^+), 281 (100), 280 (68.1), 279 (100), 216 (28.7), 171 (17), 124 (56.4), 109 (38.5%). Anal. calcd for $C_{20}H_{15}ClO_3S_2$: C, 59.62; H, 3.72%. Found C, 59.43; H, 3.68%.

3.2.6. 8-Chloro-4-(4′-chloro-3′,5′-dimethylphenoxymethyl)thiopyrano[2,3-*b*]thiochromen-5-(2*H*)-one (4f). White solid, mp 176°C; yield 80% (432 mg); UV (EtOH) λ_{max}: 212 (log ε=4.21), 261 (log ε=4.51), 353 (log ε=3.92) nm; IR (KBr) ν_{max}: 1610, 1586, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 2.29 (s, 6H, $2CH_3$), 3.42 (d, 2H. J=6.0 Hz, $-SCH_2$), 5.03 (s, 2H, $-OCH_2$), 6.12–7.47 (m, 5H, Ar*H*); 8.27 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 438 (0.75), 436 (2.2), 434 (1.9, M^+), 281 (42.6), 280 (23.2), 279 (100), 256 (21.3), 156 (36.2), 121 (44.7), 106 (24.5), 91 (29.8%). Anal. calcd for $C_{21}H_{16}Cl_2O_2S_2$: C, 57.93; H, 3.67%. Found C, 57.88; H, 3.69%.

3.3. General procedure for rearrangement of 4-(aryloxymethyl)thiopyrano[2,3-*b*]benzothiopyran-5(2*H*)ones

A mixture of compound (**4a**–**f**) (1 mmol) in *N*,*N*-diethylaniline (5 mL) was refluxed for 4–6 h. The reaction mixture was cooled, poured into ice-cold 6N HCl (30 mL), and extracted with $CHCl_3$ (3×20 mL).The $CHCl_3$ layer was washed with water and dried over Na_2SO_4. Removal of $CHCl_3$ gave a viscous liquid which was chromatographed over silica gel. Elution of the column with 50% benzene–petroleum ether furnished products **8a**–**f**.

3.3.1. 10-Chloro-5b,13b-dihydro-4,13b-dimethylbenzofuro[3,2-*c*]thiopyrano[3,2-*b*]thiochromen-13-one (8a). White solid, mp 132°C; yield 55% (212 mg); UV (EtOH) λ_{max}: 217 (log ε=4.13), 275 (log ε=4.37), 335 (log ε=4.98) nm; IR (KBr) ν_{max}: 1620, 1570, 1420 cm^{-1}; ^1H NMR (300 MHz): δ 1.78 (s, 3H, $-CH_3$ of ring junction), 2.30 (s, 3H, $ArCH_3$), 2.83–2.91 (dd, 1H, J=12.0, 13.0 Hz, $-SCH_2$), 2.98–3.04 (dd, 1H. J=4.0, 13.0 Hz, $-SCH_2$), 3.46–3.52 (dd, 1H, J=4.0, 12.0 Hz, *H* of ring junction), 6.85–7.42 (m, 5H, Ar*H*), 8.42 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 388 (43.4), 386 (100, M^+), 371 (43.2), 281 (38.6), 279 (71.2), 266 (32.3), 253 (48.8), 171 (22.3), 107 (19.2), 91 (26.3%). Anal. calcd for $C_{20}H_{15}ClO_2S_2$: C, 62.18; H, 3.89%. Found C, 62.05; H, 3.70%.

3.3.2. 10-Chloro-5b,13b-dihydro-4-chloro-13b-methylbenzofuro[3,2-*c*]thiopyrano[3,2-*b*]thiochromen-13-one (8b). White solid, mp 145°C; yield 50% (202 mg); UV (EtOH) λ_{max}: 205 (log ε=4.18), 271 (log ε=4.42), 311 (log ε=4.00)nm; IR (KBr) ν_{max}: 1620, 1580, 1450 cm^{-1}; ^1H NMR (300 MHz): δ 1.79 (s, 3H, $-CH_3$ of ring junction), 2.84–2.92 (dd, 1H, J=12.0, 13.0 Hz, $-SCH_2$), 2.99–3.05 (dd, 1H, J=4.0, 13.0 Hz, $-SCH_2$), 3.51–3.56 (dd, 1H, J=4.0, 12.0 Hz, *H* of ring junction), 6.89–7.45 (m, 5H, Ar*H*); 8.45 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI): *m/z*: 410 (23.4), 408 (71.3), 406 (100, M^+), 393 (23.4), 391 (33), 373 (19.1), 281 (24.1), 279 (59.6), 266 (70.2), 253 (47.9), 170 (21.3), 110 (19.1%). Anal. calcd for $C_{19}H_{12}Cl_2O_2S_2$: C, 56.01; H, 2.94%. Found C, 56.10; H, 3.06%.

3.3.3. 10-Chloro-5b,13b-dihydro-3,5,13b-trimethylbenzofuro[3,2-*c*]thiopyrano[3,2-*b*]thiochromen-13-one (8c). White solid, mp 194°C; yield 50% (200 mg); UV (EtOH) λ_{max}: 211 (log ε=4.14), 275 (log ε=4.38), 336 (log ε=3.95) nm; IR (KBr) ν_{max}: 1622, 1580, 1307 cm^{-1}; ^1H NMR (300 MHz): δ 1.72 (s, 3H, $-CH_3$ of ring junction); 2.28 (s, 3H, $ArCH_3$), 2.32 (s, 3H, $ArCH_3$), 2.73–2.81 (dd, 1H, J=12.0, 13.0 Hz, $-SCH_2$), 2.95–3.01 (dd, 1H, J=4.0, 13.0 Hz, $-SCH_2$), 3.42–3.47 (dd, 1H, J=4.0, 12.0 Hz, *H* of ring junction), 6.55–7.45 (m, 5H, Ar*H*); 8.46 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 402 (65.9), 400 (100,

M^+), 385 (61.7), 367 (27.7), 281 (25.5), 279 (64.9), 266 (24.5), 256 (32.9), 171 (40.4), 135 (47.9), 95 (27.7%). Anal. calcd for $C_{21}H_{17}ClO_2S_2$: C, 63.00; H, 4.25%. Found C, 63.20; H, 4.17%.

3.3.4. 10-Chloro-5b,13b-dihydro-4-tert.butyl-13b-methylbenzofuro[3,2-*c*]thiopyrano[3,2-*b*]thio-chromen-13-one (8d). White solid, mp 203°C; yield 53% (225 mg); UV (EtOH) λ_{max}: 218 (log ε=4.11), 275 (log ε=4.34), 336 (log ε=3.95) nm; IR (KBr) ν_{max}: 1625, 1582, 1299 cm^{-1}; ^1H NMR (300 MHz): δ 1.30 (s, 9H, $-C(CH_3)_3$); 1.78 (s, 3H, $-CH_3$ of ring junction), 2.85–2.93 (dd, 1H, J=12.0, 13.0 Hz, $-SCH_2$), 3.02–3.08 (dd, 1H, J=4.0, 13.0 Hz, $-SCH_2$), 3.48–3.53 (dd, 1H, J=4.0, 12.0 Hz, *H* of ring junction), 6.88–7.44 (m, 5H, Ar*H*); 8.45 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*:430 (28.7), 428 (100, M^+), 413 (81.9), 395 (20.8), 371 (34), 281 (43.6), 279 (77.6), 266 (23.4), 253 (14.9), 161 (21.3), 97 (19.1%). Anal. calcd for $C_{23}H_{21}ClO_2S_2$: C, 64.41; H, 4.90%. Found C, 64.26; H, 5.00%.

3.3.5. 10-Chloro-5b,13b-dihydro-4-methoxy-13b-methylbenzofuro[3,2-*c*]thiopyrano[3,2-*b*]thio-chromen-13-one (8e). White solid, mp 70°C; yield 50% (200 mg); UV (EtOH) λ_{max}: 217 (log ε=4.18), 275 (log ε=4.35), 336 (log ε=4.00) nm; IR (KBr) ν_{max}: 1610, 1580, 1305 cm^{-1}; ^1H NMR (300 MHz): δ 1.78 (s, 3H, $-CH_3$ of ring junction), 2.86–2.94 (dd, 1H, J=12.0, 13.0 Hz, $-SCH_2$), 3.00–3.06 (dd, 1H, J=4.0, 13.0 Hz, $-SCH_2$), 3.48–3.53 (dd, 1H, J=4.0, 12.0 Hz, *H* of ring junction), 3.77 (s, 3H, $-OCH_3$), 6.73–7.44 (m, 6H, Ar*H*), 8.44 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 404 (39.4), 402 (100, M^+), 387 (31.9), 369 (19.2), 279 (22.3), 266 (14.9), 253 (14.9), 171 (14.9), 150 (20.2), 109 (14.9%). Anal. calcd for $C_{20}H_{15}ClO_3S_2$: C, 59.62; H, 3.72%. Found C, 59.80; H, 3.60%.

3.3.6. 10-Chloro-5b,13b-dihydro-4-chloro-3,5,13b-trimethylbenzofuro[3,2-*c*]thiopyrano[3,2-*b*] thiochromen-13-one (8f). White solid, mp 192°C; yield 54% (235 mg); UV (EtOH) λ_{max}: 212 (log ε=4.18), 261 (log ε=4.42), 337 (log ε=4.00) nm; IR (KBr) ν_{max}: 1610, 1580, 1305 cm^{-1}; ^1H NMR (300 MHz): δ 1.72 (s, 3H, $-CH_3$ of ring junction), 2.34 (s, 3H, $ArCH_3$), 2.38 (s, 3H, $ArCH_3$), 2.72–2.80 (dd, 1H, J=12.0, 13.0 Hz, $-SCH_2$), 2.92–2.98 (dd, 1H, J=4.0, 13.0 Hz, $-SCH_2$), 3.43–3.48 (dd, 1H, J=4.0, 12.0 Hz, *H* of ring junction), 6.76–7.40 (m, 3H, Ar*H*), 8.44 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 438 (11.7), 436 (71.3), 434 (87.2, M^+), 419 (44.7), 401 (35.1), 281 (50), 279 (100), 266 (37.2), 253 (30.9), 169 (22.4), 97 (24.5%). Anal. calcd for $C_{21}H_{16}Cl_2O_2S_2$: C, 57.93; H, 3.67%. Found C, 57.89; H, 3.63%.

3.4. General procedure for the preparation of compound 10

Compounds **4a** (0.52 mmol) in presence of catalytic amount *N*,*N*-diethyl aniline for 14 h. The reaction mixture was then cooled and directly subjected to column chromatography over silica gel. *o*-dichlorobenzene and *N*,*N*-diethyl aniline were eluted out with petroleum ether. The product **10** was obtained when column was eluted with benzene–ethyl-acetate (19:1).

3.4.1. 8-Chloro-2,3-dihydro-4-exomethylene-3-(4′-methyl-2′-hydroxyphenyl)thiopyrano[2,3-*b*]thiochrom-4-en-5-one (10). White solid, mp 170°C; yield 40% (70 mg); UV (EtOH) λ_{max}: 208 (log ε=4.02), 220 (log ε=4.25), 357 (log ε=4.73) nm; IR (KBr) ν_{max}: 1620, 1560, 1310 cm^{-1}; ^1H NMR (300 MHz): δ 2.17 (s, 3H, $ArCH_3$), 3.30–3.64 (m, 2H, $-SCH_2$), 4.34–4.36 (m, 1H, $-SCH_2CH$), 5.19 (s, 1H, $=CH_2$), 6.08 (s, 1H, $=CH_2$), 6.60–6.72 (m, 5H, Ar*H*), 8.36–8.39 (d, 1H, J=8.5 Hz, Ar*H*); HRMS (EI) *m/z*: 388 (0.53), 386 (2.8, M^+), 256 (20.2), 149 (25.5), 141 (14.9), 129 (21.3), 113 (24.5), 111 (24.5), 97 (43.6), 85 (100%). Anal. calcd for $C_{20}H_{15}ClO_2S_2$: C, 67.70; H, 4.23%. Found C, 67.20; H, 4.00%.

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