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# Intramolecular electrophilic hydroarylation via Claisen rearrangement: synthesis of chromenes, heterothiochromenes and heterodihydrothiochromenes

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**Abstract**—We have designed and synthesized several basic and novel fused ring heterocycles by intramolecular hydroarylation with an efficiency and scope to develop intermediates of potential value. This method demonstrated consistent performance with arene–ene and arene–yne substrates of diverse structural features, including propargyl ethers, allyl thioethers, and propargyl thioethers resulting in 6-*endo* products.


## 1. Introduction

Chromene and thiochromene analogs of the HIV-1 protease inhibitor, Ritonavir, have been prepared and are under clinical trials (Fig. 1).[1,2] Some of the patents report chromene and thiochromene as modulators of the estrogen receptors.[3,4] The addition of an aromatic ring to alkenes or alkynes to form C–C bonds via C–H functionalization provides efficient and atom-economic synthetic methods. This C–C bond formation forms the basis for the synthesis of a large number of heterocycles. These seemingly simple points lead to consequences of significant importance in both the strategy and design of simple organic molecules. Intramolecular hydroarylation, a formal addition of arene C–H bonds across multiple bonds, provides a direct route to valuable organic compounds such as annulated arenes, heterocycles, and carbocycles. In contrast to the Heck reaction, a hydroarylation approach eliminates the requirement of a halogen (or triflate) substituent, which is also a feature of other routes. These alternative routes include arene metallation–Heck type addition,[5] multiple bond activation–electrophilic substitution,[6] and metal-catalyzed Claisen rearrangement.[7,8a,b] The compatibility of $Pt(IV)Cl_4$ and $Ru(III)Cl_3$ on the cyclization of alkyne substrates, specifically propargyl–aryl ethers and alkene–aryl ethers, by multiple bond activation–electrophilic substitution have been studied.[9a,b] Cyclization via Claisen rearrangement carried out under harsh conditions is also described (Scheme 1).[9a] The thermal rearrangement of phenol **D** at 240 °C resulted into **E** and **F** in a 7:3 ratio. In contrast, substrate **D** in the presence of 2 mol % of $PtCl_4$ in dioxane at ambient temperature afforded **E** in 59% yield, whereas isomer **F** was not detected in the crude reaction mixture. Many more studies with regard to the development of catalysts for the hydroarylation reaction of alkynes and olefins have been reported.[10–19]

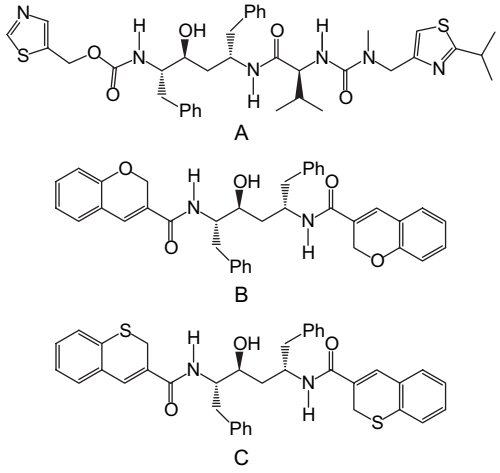


**Figure 1**. A is the HIV-1 protease inhibitor Ritonavir, B and C are chromene and thiochromene analogs of Ritonavir.

*Keywords*: Hydroarylation; Claisen rearrangement; Pyran; Thiopyran; Dihydrothiopyran; Chromene.
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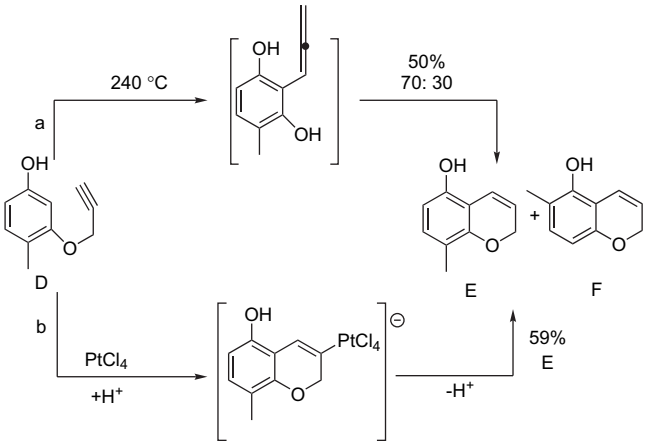
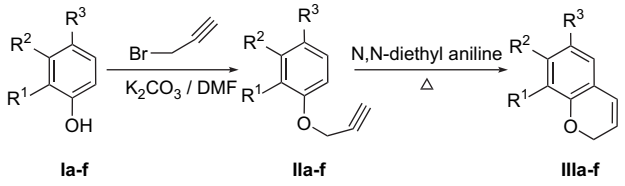



**Scheme 1**. Conditions: (a) 240 °C, diethyleneglycol; (b) 2 mol % $PtCl_4$, dioxane, rt.

## 2. Results and discussion

Initially we became interested in the possibility of making simple moieties, which could be the basic framework for various active ingredients of unexplored physiological and pharmaceutical interest. For the synthesis of the desired molecules, various phenols were reacted with propargyl bromides in the presence of base to synthesize propargyl–aryl ethers. The heteroaromatic compounds were first treated with *n*-butyllithium and sulfur to give the thiolate salt formed in situ, these were then reacted with propargyl and alkenyl bromides to give propargyl and alkenyl thioethers. Propargyl ethers underwent cyclization to give the desired products when heated in *N*,*N*-diethylaniline as solvent and base, whereas the alkenyl thioethers underwent cyclization by heating in *N*,*N*-dimethylformamide. For the cyclization of propargyl thioethers either *N*,*N*-diethylaniline or *N*,*N*-dimethylformamide is used. The yields obtained are much higher following our method of synthesis than those reported when the cyclizations were carried out using transition metal salts.[9a,b] In our first attempt we have synthesized some fused ring heterocycles from various phenol derivatives as depicted in Scheme 2. The hydroxyl derivatives **Ia–f** were reacted with propargyl bromide in the presence of potassium carbonate to give the propargyl–aryl ethers **IIa–f**. The resulting intermediates **IIa–f** were then heated in *N*,*N*-diethylaniline




**Ia, IIa, IIIa**:- $R^1$ = Ph, $R^2$ = $R^3$ = H
**Ib, IIb, IIIb**:- $R^2$ = Ph, $R^1$ = $R^3$ = H
**Ic, IIc, IIIc**:- $R^3$ = Ph, $R^1$ = $R^2$ = H
**Id, IId, IIId**:- $R^3$ = 4-BrPh, $R^1$ = $R^2$ = H
**Ie, IIe, IIIe**:- $R^1$-$R^2$ =  $R^3$ = H
**If, IIf, IIIf** :- $R^1$-$R^2$ =  $R^3$ = H

**Scheme 2**.

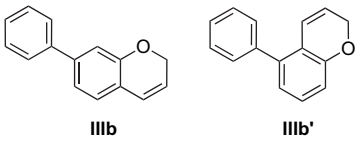
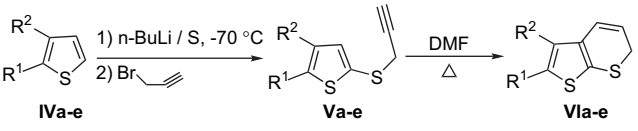



**Figure 2**.

at 220 °C and underwent rearrangement to give the fused ring pyran derivatives **IIIa–f**. It is possible that one of the propargyl ethers (e.g., 1-phenyl-3-(2-propynyloxy)benzene **IIb**) could upon cyclization give rise to either chromene **IIIb** and/or **IIIb′** (Fig. 2), however, under our reaction conditions only formation of chromene **IIIb** was ever observed.

With the establishment of an exciting lead, we were prepared to determine the efficacy of synthesizing thiopyran and dihydrothiopyran derivatives by following the route depicted in Schemes 3 and 4. Thiophenes **IVa–f** were reacted with *n*-butyllithium and sulfur at −70 °C to give the thiolate salts, which were then reacted in situ with propargyl bromide and α-(bromomethyl)-acrylic acid[21] to give 2-propynylsulfanyl thiophenes **Va–e** and 2-acryloylsulfanyl thiophenes **VIIa–e**, respectively. The conversion of the intermediates to the final thiopyrans **VIa–e** and dihydrothiopyrans **VIIIa–e** was achieved by heating at 145 °C in DMF for 45 min. 5,6-Dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid **VIIIa** has been reported as a starting material for the synthesis of presynaptic dopamine receptors.[20]



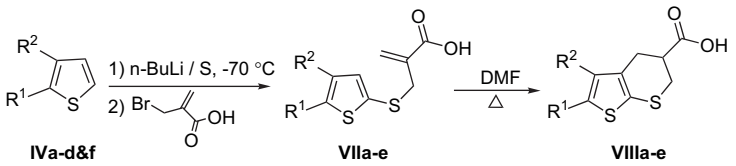

**IVa, Va, VIa**:- $R^1$ = $R^2$ = H. **IVb, Vb, VIb**:- $R^1$ = Me, $R^2$ = H.
**IVc, Vc, VIc**:- $R^1$ = Et, $R^2$ = H. **IVd, Vd, VId**:- $R^1$ = n-Pr, $R^2$ = H.
**IVe, Ve, VIe**:- $R^1$-$R^2$ = Benzo.

**Scheme 3**.

After successfully synthesizing the thiophene fused ring thiopyran and dihydrothiopyran we diverted our research interest to the synthesis of dibenzofuran and dibenzothiophene derivatives as depicted in Scheme 5. Dibenzofuran and dibenzothiophene were reacted with *n*-butyllithium resulting in mono-lithium salts,[22] which were then treated with sulfur at lower temperatures to give the *S*-lithium salts. These were then reacted with bromides at the same temperature to give the intermediate thioethers **Xa**,**b** and **XIIa**,**b**. The intermediate thioethers were then heated in *N*,*N*-diethylaniline or *N*,*N*-dimethylformamide to give the cyclized products **XIa**,**b** and **XIIIa**,**b** as depicted in Scheme 5.

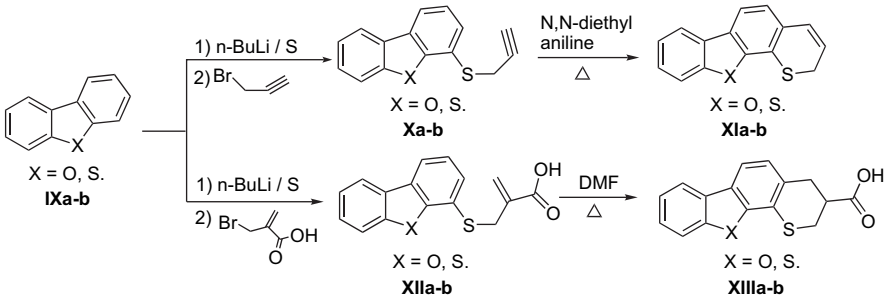
## 3. Conclusions

We have synthesized a large number of novel heterocyclic systems by means of Claisen rearrangement methodology. The systems developed can give access to a large number of compounds for biological testing.




**IVa, VIIa, VIIIa**:- $R^1 = R^2 = H$. **IVb, VIIb, VIIIb**:- $R^1$ = Me, $R^2 = H$.
**IVc, VIIc, VIIIc**:- $R^1$ = Et, $R^2 = H$. **IVd, VIId, VIIId**:- $R^1$ = n-Pr, $R^2 = H$.
**IVf, VIIe, VIIIe**:- $R^1$ = CN, $R^2 = H$.

**Scheme 4**.




**Scheme 5**.

## 4. Experimental

### 4.1. General

The 2-, 3- and 4-phenylphenols **Ia–c** and 4-bromo-4-hydroxy biphenyl **Id** required for the synthesis were purchased. 4-Hydroxydibenzofuran **Ie** and 4-hydroxydibenzothiophene **If** were synthesized according to the method reported in the literature.[22a–c] Thiophenes **IVa–f** required for the synthesis were purchased. Melting points are uncorrected, measured on a Büchi apparatus. Infrared spectra were recorded on a FTIR Perkin–Elmer spectrometer. $^1$H NMR spectra were recorded using a 300 MHz Varien (Mercury Vx) SWBB Multinuclear Probe with tetramethylsilane (TMS) as the internal standard. Mass spectra were recorded on a MDS Sciex API 3000 LCMS.

### 4.2. General method for the synthesis of 2-propynyloxy aryl derivatives IIa–f. Procedure A

**4.2.1. 1-Phenyl-2-(2-propynyloxy)benzene IIa.** Propargyl bromide (0.40 g, 3.33 mmol) was added to a mixture of 2-phenylphenol (0.51 g, 3.0 mmol) and $K_2CO_3$ (0.48 g, 3.5 mmol) in dry DMF (10 mL) and stirred at room temperature for 2 h under a nitrogen atmosphere. DMF was then removed under reduced pressure and the residue dissolved in 50 mL of ethyl acetate. The organic layer was washed with water (2×25 mL), dried over sodium sulfate and concentrated under reduced pressure to give pure 1-phenyl-2-(2-propynyloxy)benzene **IIa** (0.625 g, 100%) as a gummy oil; [Found: C, 86.30; H, 5.93. $C_{15}H_{12}O$ requires: C, 86.51; H, 5.81]; IR (neat): 3289, 3061, 1503, 1480, 1434, 1266, 1210, 1123, 1023, and 1009 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 2.54 (t, $J$ 2.4 Hz, 1H), 4.66 (d, $J$ 2.4 Hz, 2H), 7.04–7.14 (m, 2H), 7.28–7.42 (m, 5H), 7.50–7.54 (m, 2H).

**4.2.2. 1-Phenyl-3-(2-propynyloxy)benzene IIb.** Compound **IIb** was prepared from 3-phenylphenol **Ib** (0.51 g, 3.0 mmol) in an analogous manner to that for the preparation of **IIa** as a colorless oil (0.625 g, 100%); [Found: C, 86.33; H, 5.90. $C_{15}H_{12}O$ requires: C, 86.51; H, 5.81]; IR (neat): 3303, 3015, 1597, 1573, 1478, 1422, 1295, 1215, 1197, and 1035 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 2.54 (t, $J$ 2.4 Hz, 1H), 4.75 (d, $J$ 2.4 Hz, 2H), 6.95 (dd, $J$ 3.2 Hz, 1H), 7.20–7.24 (m, 2H), 7.32–7.46 (m, 4H), 7.52–7.59 (m, 2H).

**4.2.3. 1-Phenyl-4-(2-propynyloxy)benzene IIc.** Compound **IIc** was prepared from 4-phenylphenol **Ic** (0.51 g, 3.0 mmol) in an analogous manner to that for the preparation of **IIa** as a white solid (0.59 g, 95%), mp=75–78 °C; [Found: C, 86.42; H, 5.69. $C_{15}H_{12}O$ requires: C, 86.51; H, 5.81]; IR (KBr): 3275, 3303, 1603, 1584, 1519, 1486, 1287, 1237, 1118, and 1027 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): $\delta$ 3.59 (t, $J$ 2.4 Hz, 1H), 4.83 (d, $J$ 2.4 Hz, 2H), 7.04–7.08 (m, 2H), 7.29(t, $J$ 2.4 Hz, 1H), 7.41 (d, $J$ 7.2 Hz, 2H), 7.41 (d, $J$ 8.4 Hz, 4H).

**4.2.4. 1-(4-Bromophenyl)-4-(2-propynyloxy)benzene IId.** Compound **IId** was prepared from 4-(4-bromophenyl)phenol **Id** (0.75 g, 3.0 mmol) in an analogous manner to that for the preparation of **IIa** as a white solid (0.82 g, 97%), mp=93–95 °C; [Found: C, 62.65; H, 3.99; Br, 27.62. $C_{15}H_{11}BrO$ requires: C, 62.74; H, 3.86; Br, 27.83]; IR (KBr): 3282, 2915, 1602, 1580, 1518, 1480, 1376, 1283, 1240, 1076, 1027, 817, and 805 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 2.55 (t, $J$ 2.4 Hz, 1H), 4.75 (d, $J$ 2.4 Hz, 2H), 7.06 (d, $J$ 7.8 Hz, 2H), 7.42 (d, $J$ 7.8 Hz, 2H), 7.50–7.58 (m, 4H).

**4.2.5. 4-(2-Propynyloxy)dibenzo[*b*,*d*]furan IIe.** Compound **IIe** was prepared from 4-hydroxydibenzo[*b*,*d*]furan

**IIe** (0.55 g, 3.0 mmol) in an analogous manner to that for the preparation of **IIa**, and the crude semisolid obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% ethyl acetate in hexane) as a white solid (0.62 g, 93%), mp=32–34 °C; [Found: C, 81.30; H, 4.66. $C_{15}H_{10}O_2$ requires: C, 81.07; H, 4.54]; IR (KBr): 3293, 2923, 1583, 1451, 1310, 1191, 1092, 1022, and 932 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.63 (t, *J* 2.4, 2.4 Hz, 1H), 5.05 (d, *J* 2.4 Hz, 2H), 7.20 (d, *J* 7.2 Hz, 1H), 7.33 (t, *J* 7.8, 7.8 Hz, 1H), 7.40 (t, *J* 6.9, 6.9 Hz, 1H), 7.52 (t, *J* 6.9, 6.9 Hz, 1H), 7.66 (dd, *J* 1.0, 1.0 Hz, 1H), 7.70 (d, *J* 7.2, 1H), 8.00 (dd, *J* 1.0, 1.0 Hz, 1H).

**4.2.6. 4-(2-Propynyloxy)dibenzo[*b*,*d*]thiophene IIf.** Compound **IIf** was prepared from 4-hydroxydibenzo[*b*,*d*]thiophene **IIf** (0.60 g, 3.0 mmol) in an analogous manner to that for the preparation of **IIa**, and the crude semisolid obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% ethyl acetate in hexane) as a white solid (0.60 g, 84%), mp=109–110 °C; [Found: C, 75.79; H, 4.11; S, 13.58. $C_{15}H_{10}OS$ requires: C, 75.60; H, 4.23; S, 13.45]; IR (KBr): 3305, 1568, 1445, 1321, 1271, 1233, 1107, 1061, 1010, and 927 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.55 (t, *J* 2.4 Hz, 1H), 4.91 (d, *J* 2.4 Hz, 2H), 7.05 (d, *J* 7.5 Hz, 1H), 7.38–7.46 (m, 3H), 7.85 (dd, *J* 0.9, 0.9 Hz, 1H), 7.86 (d, *J* 7.5 Hz, 1H), 8.10 (d, *J* 7.5 Hz, 1H).

### 4.3. General method for the synthesis of chromene derivatives IIIa–f. Procedure B

**4.3.1. 8-Phenyl-2*H*-chromene IIIa.** 1-Phenyl-2-(2-propynyloxy)benzene **IIa** (0.370 g, 1.78 mmol) was taken up in *N*,*N*-diethylaniline (20 mL) and stirred at a temperature of 230–240 °C for 18 h under a nitrogen atmosphere. It was then cooled to room temperature and diluted with ethyl acetate (50 mL), washed three times with 50 mL of 2 N aq HCl, and then two times with 25 mL of brine. The organic layer was dried over sodium sulfate and concentrated under reduced pressure to give crude **IIIa**. The crude compound was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 15% chloroform in hexane) to give 8-phenyl-2*H*-chromene **IIIa** (0.10 g, 27%) as a white gummy semisolid; [Found: C, 86.41; H, 5.70. $C_{15}H_{12}O$ requires: C, 86.51; H, 5.81]; IR (neat): 2918, 1461, 1429, 1212, 1110, 1070, and 1035 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 4.80 (dd, *J* 2.1, 2.1 Hz, 2H), 5.82 (dt, *J* 3.6, 2.4 Hz, 1H), 6.48 (d, *J* 9.5 Hz, 1H), 6.90–6.98 (m, 2H), 7.17 (dd, *J* 2.4, 2.4 Hz, 1H), 7.29 (d, *J* 7.4 Hz, 1H), 7.38–7.43 (m, 2H), 7.53 (d, *J* 8.0 Hz, 2H). MS (EI) *m*/*z* 207.2 ($M^{-1}$).

**4.3.2. 7-Phenyl-2*H*-chromene IIIb.** Compound **IIIb** was prepared from 1-phenyl-3-(2-propynyloxy)benzene **IIb** (0.370 g, 1.78 mmol) in an analogous manner to that for the preparation of **IIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 5% chloroform in hexane) as a gummy oil (0.11 g, 30%); [Found: C, 86.66; H, 5.99. $C_{15}H_{12}O$ requires: C, 86.51; H, 5.81]; IR (neat): 2189, 1596, 1463, 1435, 1237, 1200, 1116, and 1018 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 4.79 (dd, *J* 2.1, 2.1 Hz, 2H), 5.77 (dt, *J* 3.0, 2.2 Hz, 1H), 6.43 (d, *J* 9.5 Hz, 1H), 6.83 (d, *J* 8.1 Hz, 1H), 6.89 (d, *J* 8.0 Hz, 1H), 7.16 (t, *J* 7.5, 7.5 Hz, 1H), 7.33–7.45 (m, 5H). MS (EI) *m*/*z* 207.2 ($M^{-1}$).

**4.3.3. 6-Phenyl-2*H*-chromene IIIc.** Compound **IIIc** was prepared from 1-phenyl-4-(2-propynyloxy)benzene **IIc** (0.370 g, 1.78 mmol) in an analogous manner to that for the preparation of **IIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 15% chloroform in hexane) as a white solid (0.20 g, 55%); mp=78–80 °C; [Found: C, 86.69; H, 5.65. $C_{15}H_{12}O$ requires: C, 86.51; H, 5.81]; IR (KBr): 3050, 2832, 1480, 1452, 1231, 1184, 1135, 1047, 1016, 891, and 836 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 4.85 (dd, *J* 1.8, 1.8 Hz, 2H), 5.80 (dt, *J* 3.5, 2.4 Hz, 1H), 6.46 (d, *J* 9.6 Hz, 1H), 6.82 (d, *J* 8.4 Hz, 1H), 7.17 (d, *J* 8.0 Hz, 1H), 7.24–7.28 (m, 2H), 7.39 (t, *J* 7.4, 7.4 Hz, 2H), 7.50 (d, *J* 8.0 Hz, 2H). MS (EI) *m*/*z* 207.4 ($M^{-1}$).

**4.3.4. 6-(4-Bromophenyl)-2*H*-chromene IIId.** Compound **IIId** was prepared from 1-(4-bromophenyl)-4-(2-propynyloxy)benzene **IId** (0.43 g, 1.5 mmol) in an analogous manner to that for the preparation of **IIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 5% chloroform in hexane) as a white solid (0.27 g, 63%); mp=107–110 °C; [Found: C, 62.83; H, 3.69; Br, 27.70. $C_{15}H_{11}BrO$ requires: C, 62.74; H, 3.86; Br, 27.83]; IR (KBr): 3282, 2915, 1602, 1518, 1480, 1376, 1283, 1240, 1196, and 1076 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 4.87 (dd, *J* 1.8, 1.8 Hz, 2H), 5.82 (dt, *J* 3.6, 2.4 Hz, 1H), 6.49 (d, *J* 9.0 Hz, 1H), 6.80 (d, *J* 8.0 Hz, 1H), 7.25–7.28 (m, 2H), 7.35–7.41 (m, 2H), 7.48–7.55 (d, *J* 8.0 Hz, 2H). MS (EI) *m*/*z* 287.0 ($M^+$).

**4.3.5. 2*H*-Benzo[4,5]furo[3,2-*h*]chromene IIIe.** Compound **IIIe** was prepared from 4-(2-propynyloxy)dibenzo[*b*,*d*]furan **IIe** (0.45 g, 2.0 mmol) in an analogous manner to that for the preparation of **IIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% ethyl acetate in hexane) as a pale yellow solid (0.29 g, 65%); mp=68–70 °C; [Found: C, 80.90; H, 4.38. $C_{15}H_{10}O_2$ requires: C, 81.07; H, 4.54]; IR (KBr): 2921, 1497, 1427, 1306, 1228, 1191, 1665, 1012, and 930 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 5.03 (dd, *J* 2.1, 2.1 Hz, 2H), 5.82 (dt, *J* 3.2, 2.0 Hz, 1H), 6.56 (d, *J* 9.0 Hz, 1H), 6.95 (d, *J* 7.8 Hz, 1H), 7.31 (t, *J* 5.9, 5.9 Hz, 1H), 7.43–7.46 (m, 2H), 7.56 (d, *J* 7.8 Hz, 1H), 7.87 (d, *J* 7.8 Hz, 1H). MS (EI) *m*/*z* 223.3 ($M^{+1}$).

**4.3.6. 2*H*-Benzo[4,5]thieno[3,2-*h*]chromene IIIf.** Compound **IIIf** was prepared from 4-(2-propynyloxy)dibenzo[*b*,*d*]thiophene **IIf** (0.475 g, 2.0 mmol) in an analogous manner to that for the preparation of **IIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% ethyl acetate in hexane) as a white solid (0.33 g, 70%); mp=88–90 °C; [Found: C, 75.42; H, 4.05; S, 13.29. $C_{15}H_{10}OS$ requires: C, 75.60; H, 4.23; S, 13.45]; IR (KBr): 2923, 1553, 1483, 1406, 1249, 1202, 1131, 1063, 1016, and 813 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 5.30 (dd, *J* 2.1, 2.1 Hz, 2H), 5.78 (dt, *J* 3.6, 2.3 Hz, 1H), 6.52 (d, *J* 9.2 Hz, 1H), 7.05 (d, *J* 7.8 Hz, 1H), 7.37–7.42 (m, 2H), 7.64 (d, *J* 7.8 Hz, 1H), 7.82 (d, *J* 8.0 Hz, 1H), 8.05 (d, *J* 8.0 Hz, 1H). MS (EI) *m*/*z* 238.9 ($M^{+1}$).

### 4.4. General method for the synthesis of 2-(2-propynylsulfanyl)thiophene and benzothiophene derivatives Va–f. Procedure C

**4.4.1. 2-(2-Propynylsulfanyl)thiophene Va.** A solution of *n*-butyllithium (13.34 $cm^3$ of 15% in *n*-hexane, 31.25 mmol) was added to a solution of thiophene **IVa** (2.0 g, 23.8 mmol) in dry THF (20 mL) at −70 °C for a period of 10 min and stirred at −70 to −60 °C for 30 min under a nitrogen atmosphere. Granular sulfur (0.76 g, 23.8 mmol) was added in one portion and then the reaction mixture was stirred at −70 to −60 °C for another 30 min. A cold solution of propargyl bromide (3.11 g, 26.2 mmol) dissolved in dry THF (10 mL) was added so as to maintain the temperature between −70 and −60 °C. After the addition was complete the temperature was gradually raised to −30 °C over a period of 1 h. Reaction was quenched with 2 N cold dilute HCl solution. The mixture was extracted with ethyl acetate (2×100 mL) and the combined organic layers were washed with water (2×100 mL), saturated sodium bicarbonate (100 mL) followed by brine solution (100 mL) and dried over sodium sulfate. This organic layer was concentrated to give the crude product, which was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% ethyl acetate in hexane) to give 2-(2-propynylsulfanyl)thiophene **Va** (1.8 g, 49%) as a viscous oil; [Found: C, 54.73; H, 4.03; S, 41.79. $C_7H_6S_2$ requires: C, 54.51; H, 3.92; S, 41.57]; IR (neat): 3292, 2919, 1594, 1438, 1226, 1213, 953, and 798 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.28 (t, *J* 2.4, 2.4 Hz, 1H), 3.46 (d, *J* 2.4 Hz, 2H), 7.00 (dd, *J* 1.8, 1.8 Hz, 1H), 7.25 (dd, *J* 0.9, 0.9 Hz, 1H), 7.49 (dd, *J* 0.9, 0.9 Hz, 1H).

**4.4.2. 2-Methyl-5-(2-propynylsulfanyl)thiophene Vb.** Compound **Vb** was prepared from 2-methylthiophene **IVb** (2.35 g, 23.8 mmol) in an analogous manner to that for the preparation of **Va**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (2.1 g, 53%); [Found: C, 57.33; H, 4.62; S, 38.33. $C_8H_8S_2$ requires: C, 57.10; H, 4.79; S, 38.11]; IR (neat): 3309, 3018, 1439, 1215, 1161, 1068, and 953 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.27 (t, *J* 2.4, 2.4 Hz, 1H), 2.45 (s, 3H), 3.41 (d, *J* 3.0 Hz, 2H), 6.64 (d, *J* 4.2 Hz, 1H), 7.05 (d, *J* 4.2 Hz, 1H).

**4.4.3. 2-Ethyl-5-(2-propynylsulfanyl)thiophene Vc.** Compound **Vc** was prepared from 2-ethylthiophene **IVc** (2.67 g, 23.8 mmol) in an analogous manner to that for the preparation of **Va**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (2.3 g, 54%); [Found: C, 59.15; H, 5.64; S, 35.42. $C_9H_{10}S_2$ requires: C, 59.30; H, 5.53; S, 35.18]; IR (neat): 3293, 2968, 1456, 1439, 1226, 1073, 981, and 805 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 1.28 (t, *J* 7.2, 7.2 Hz, 3H), 2.28 (t, *J* 2.4, 2.4 Hz, 1H), 2.82 (q, *J* 7.5, 6.8, 7.5 Hz, 2H), 3.43 (d, *J* 3.0 Hz, 2H), 6.68 (d, *J* 4.0 Hz, 1H), 7.08 (d, *J* 4.0 Hz, 1H).

**4.4.4. 2-Propyl-5-(2-propynylsulfanyl)thiophene Vd.** Compound **Vd** was prepared from 2-propylthiophene **IVd** (3.0 g, 23.8 mmol) in an analogous manner to that for the preparation of **Va**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (3.87 g, 83%); [Found: C, 61.38; H, 6.03; S, 32.45. $C_{10}H_{12}S_2$ requires: C, 61.18; H, 6.16; S, 32.66]; IR (neat): 3294, 2960, 1455, 1437, 1226, 977, and 801 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.97 (t, *J* 7.2, 7.2 Hz, 3H), 1.68 (sextet, *J* 2.3 Hz, 2H), 2.18 (t, *J* 2.4, 2.4 Hz, 1H), 2.74 (t, *J* 7.8, 7.8 Hz, 2H), 3.43 (d, *J* 2.9 Hz, 2H), 6.66 (d, *J* 3.6 Hz, 1H), 7.07 (d, *J* 3.6 Hz, 1H).

**4.4.5. 2-(2-Propynylsulfanyl)benzo[*b*]thiophene Ve.** Compound **Ve** was prepared from benzo[*b*]thiophene **IVe** (3.2 g, 23.8 mmol) in an analogous manner to that for the preparation of **Va**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (3.88 g, 80%); [Found: C, 64.46; H, 3.87; S, 31.15. $C_{11}H_8S_2$ requires: C, 64.67; H, 3.95; S, 31.39]; IR (neat): 3306, 2923, 1423, 1215, 1156, 1081, 972, and 831 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.30 (t, *J* 3.0, 3.0 Hz, 1H), 3.60 (d, *J* 2.4 Hz, 2H), 7.30–7.35 (m, 2H), 7.45 (s, 1H), 7.70–7.76 (m, 2H).

### 4.5. General method for the synthesis of 6*H*-thieno[1,3-*b*]thiopyran and 2*H*-benzo[4,5]thieno[2,3-*b*]thiopyran derivatives VIa–e. Procedure D

**4.5.1. 6*H*-Thieno[1,3-*b*]thiopyran VIa.** 2-(2-Propynylsulfanyl)thiophene **Va** (0.2 g, 1.29 mmol) was taken up in dry *N*,*N*-dimethylformamide (5 mL) and stirred at 150 °C for 30 min under a nitrogen atmosphere. Then *N*,*N*-dimethylformamide was evaporated under reduced pressure and the residue was dissolved in ethyl acetate (50 mL). The ethyl acetate layer was washed with water (2×25 mL), followed by brine (25 mL). The organic layer was dried over sodium sulfate and concentrated to give the crude compound as an oil. This crude compound was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% ethyl acetate in hexane) to give 6*H*-thieno[1,3-*b*]thiopyran **VIa** (140 mg, 70%) as a viscous oil; [Found: C, 54.39; H, 3.78; S, 41.75. $C_7H_6S_2$ requires: C, 54.51; H, 3.92; S, 41.57]; IR (neat): 3037, 2878, 1613, 1406, 1207, 1042, and 874 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 3.48 (dd, *J* 1.5, 1.5 Hz, 2H), 5.71 (dt, *J* 3.6, 2.4 Hz, 1H), 6.50 (d, *J* 7.4 Hz, 1H), 6.85 (d, *J* 5.4 Hz, 1H), 7.00 (d, *J* 5.4 Hz, 1H). MS (EI) *m*/*z* 153.3 ($M^{-1}$).

**4.5.2. 2-Methyl-6*H*-thieno[1,3-*b*]thiopyran VIb.** Compound **VIb** was prepared from 2-methyl-5-(2-propynylsulfanyl)thiophene **Vb** (0.34 g, 2.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (0.235 g, 70%); [Found: C, 56.88; H, 4.65; S, 37.85. $C_8H_8S_2$ requires: C, 57.10; H, 4.79; S, 38.11]; IR (neat): 2918, 1436, 1378, 1196, 1120, 1062, and 962 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.41 (s, 3H), 3.45 (dd, *J* 1.5, 1.5 Hz, 2H), 5.66 (dt, *J* 3.4, 2.4 Hz, 1H), 6.40 (d, *J* 7.4 Hz, 1H), 6.53 (s, 1H). MS (EI) *m*/*z* 167.0 ($M^{-1}$).

**4.5.3. 2-Ethyl-6*H*-thieno[1,3-*b*]thiopyran VIc.** Compound **VIc** was prepared from 2-ethyl-5-(2-propynylsulfanyl)thiophene **Vc** (0.36 g, 2.0 mmol) in an analogous manner to

that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (0.27 g, 75%); [Found: C, 59.06; H, 5.45; S, 35.01. $C_9H_{10}S_2$ requires: C, 59.30; H, 5.53; S, 35.18]; IR (neat): 2969, 1450, 1414, 1215, 1185, 1065, and 836 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 1.34 (t, *J* 7.5, 7.5 Hz, 3H), 2.28 (q, *J* 7.5, 6.5, 7.5 Hz, 2H), 3.53 (dd, *J* 1.5, 1.5 Hz, 2H), 5.74 (dt, *J* 3.6, 2.2 Hz, 1H), 6.48 (d, *J* 7.4 Hz, 1H), 6.63 (s, 1H). MS (EI) *m*/*z* 181.3 ($M^{-1}$).

**4.5.4. 2-Propyl-6*H*-thieno[1,3-*b*]thiopyran VId.** Compound **VId** was prepared from 2-propyl-5-(2-propynylsulfanyl)thiophene **Vd** (0.39 g, 2.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a viscous oil (0.3 g, 75%); [Found: C, 61.36; H, 6.25; S, 32.90. $C_{10}H_{12}S_2$ requires: C, 61.18; H, 6.16; S, 32.66]; IR (neat): 2917, 1441, 1314, 1212, 1131, 964, and 912 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.96 (t, *J* 7.2, 7.2 Hz, 3H), 1.65 (sextet, *J* 3.0 Hz, 2H), 2.68 (t, *J* 7.8, 7.8 Hz, 2H), 3.46 (dd, *J* 1.4, 1.4 Hz, 2H), 5.67 (dt, *J* 3.6, 2.4 Hz, 1H), 6.41 (d, *J* 8.0 Hz, 1H), 6.54 (s, 1H). MS (EI) *m*/*z* 195.1 ($M^{-1}$).

**4.5.5. 2*H*-Benzo[4,5]thieno[2,3-*b*]thiopyran VIe.** Compound **VIe** was prepared from 2-(2-propynylsulfanyl)-benzo[*b*]thiophene **Ve** (0.41 g, 2.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 10% chloroform in hexane) as a white solid (0.3 g, 75%); mp=88–90 °C; [Found: C, 64.49; H, 4.08; S, 31.55. $C_{11}H_8S_2$ requires: C, 64.67; H, 3.95; S, 31.39]; IR (KBr): 2880, 1457, 1420, 1312, 1247, 1133, 1092, and 1014 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 3.58 (dd, *J* 1.8, 1.8 Hz, 2H), 5.81 (dt, *J* 3.6, 2.5 Hz, 1H), 6.75 (d, *J* 8.0 Hz, 1H), 7.24 (t, *J* 6.6, 6.6 Hz, 1H), 7.32 (t, *J* 6.6, 6.6 Hz, 1H), 7.69 (d, *J* 7.8 Hz, 1H), 7.79 (d, *J* 7.8 Hz, 1H), MS (EI) *m*/*z* 203.3 ($M^{-1}$).

### 4.6. General method for the synthesis of 2-(2-thienyl sulfanylmethyl)acrylic acid derivatives VIIa–e

The 2-(2-thienyl sulfanylmethyl)acrylic acid derivatives **VIIa–e** were synthesized following the general procedure C from thiophenes **IVa–d** and **IVf**, α-(bromomethyl)acrylic, acid and sulfur in the presence of *n*-butyllithium as base.

**4.6.1. 2-(2-Thienyl sulfanylmethyl)acrylic acid VIIa.**[20] A solution of *n*-butyllithium (13.34 $cm^3$ of 15% in *n*-hexane, 31.25 mmol) was added to a solution of thiophene **IVa** (2.0 g, 23.8 mmol) in dry THF (20 mL) at −78 °C for a period of 10 min and stirred at −78 °C for 30 min under a nitrogen atmosphere. Granular sulfur (0.762 g, 23.8 mmol) was added in one portion and then the reaction mixture was stirred at −78 °C for another 30 min. A cold solution of α-(bromomethyl)acrylic acid (4.32 g, 26.2 mmol) dissolved in a solution of sodium hydroxide (2.2 g, 55 mmol) in water (20 mL) is then added slowly while maintaining the temperature at −78 °C. After the addition is complete the temperature is gradually raised to −30 °C over a period of 1 h. Then the reaction was quenched with 2 N cold dilute HCl solution till pH was acidic. The mixture was extracted with ethyl acetate (2×100 mL) and the combined organic layers were washed with water (2×50 mL) and dried over sodium sulfate. This organic layer was concentrated to give the crude product, which was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (3.42 g, 72%); mp=84–86 °C; [Found: C, 47.76; H, 4.18; S, 32.27. $C_8H_8O_2S_2$ requires: C, 47.98; H, 4.03; S, 32.02]; IR (neat): 3031, 2629, 1685, 1622, 1443, 1402, and 1231 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 3.59 (s, 2H), 5.88 (s, 1H), 6.24 (s, 1H), 6.95 (t, *J* 4.5, 4.5 Hz, 1H), 7.08 (d, *J* 4.2 Hz, 1H), 7.34 (d, *J* 5.1 Hz, 1H).

**4.6.2. 2-(5-Methyl-2-thienyl sulfanylmethyl)acrylic acid VIIb.** Compound **VIIb** was prepared from 2-methylthiophene **IVb** (2.35 g, 23.8 mmol) in an analogous manner to that for the preparation of **VIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (3.56 g, 70%); mp=157–160 °C; [Found: C, 50.23; H, 4.55; S, 29.70. $C_9H_{10}O_2S_2$ requires: C, 50.44; H, 4.70; S, 29.92]; IR (KBr): 2632, 1687, 1622, 1445, 1408, and 1232 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 2.44 (s, 3H), 3.54 (s, 2H), 5.38 (s, 1H), 6.24 (s, 1H), 6.60 (d, *J* 4.8 Hz, 1H), 6.87 (d, *J* 4.2 Hz, 1H).

**4.6.3. 2-(5-Ethyl-2-thienyl sulfanylmethyl)acrylic acid VIIc.** Compound **VIIc** was prepared from 2-ethylthiophene **IVc** (2.67 g, 23.8 mmol) in an analogous manner to that for the preparation of **VIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (3.8 g, 70%); mp=67–68 °C; [Found: C, 52.84; H, 5.45; S, 28.27. $C_{10}H_{12}O_2S_2$ requires: C, 52.60; H, 5.30; S, 28.09]; IR (KBr): 2965, 2629, 1691, 1622, 1440, 1323, 1218, and 926 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 1.28 (t, *J* 7.5, 7.5 Hz, 3H), 2.80 (q, *J* 7.5, 6.6, 7.5 Hz, 2H), 3.55 (s, 2H), 5.39 (s, 1H), 6.24 (s, 1H), 6.63 (d, *J* 3.6 Hz, 1H), 6.90 (d, *J* 3.6 Hz, 1H).

**4.6.4. 2-(5-Propyl-2-thienyl sulfanylmethyl)acrylic acid VIId.** Compound **VIId** was prepared from 2-propylthiophene **IVd** (3.0 g, 23.8 mmol) in an analogous manner to that for the preparation of **VIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (3.45 g, 60%); mp=61–62 °C; [Found: C, 54.32; H, 5.68; S, 26.34. $C_{11}H_{14}O_2S_2$ requires: C, 54.51; H, 5.82; S, 26.46]; IR (KBr): 2958, 2629, 1693, 1622, 1441, 1325, and 1230 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 0.97 (t, *J* 7.5, 7.5 Hz, 3H), 1.68 (sextet, *J* 2.9 Hz, 2H), 2.74 (t, *J* 7.2, 7.2 Hz, 2H), 3.56 (s, 2H), 5.38 (s, 1H), 6.24 (s, 1H), 6.64 (d, *J* 2.7 Hz, 1H), 6.91 (d, *J* 3.6 Hz, 1H).

**4.6.5. 2-(5-Cyano-2-thienyl sulfanylmethyl)acrylic acid VIIe.** Compound **VIIe** was prepared from 2-cyanothiophene **IVf** (2.6 g, 23.8 mmol) in an analogous manner to that for the preparation of **VIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (2.73 g, 51%); mp=94–96 °C; [Found: C, 47.76; H, 3.27; N, 6.02; S, 28.65. $C_9H_7NO_2S_2$ requires: C,

47.98; H, 3.13; N, 6.22; S, 28.46]; IR (KBr): 2880, 2522, 2222,1687, 1622, 1440, 1417, 1311, and 1215 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 3.70 (s, 2H), 5.56 (s, 1H), 6.32 (s, 1H), 7.04 (d, *J* 3.9 Hz, 1H), 7.24 (d, *J* 4.2 Hz, 1H).

### 4.7. General method for the synthesis of 5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid derivatives VIIIa–e

5,6-Dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acids **VIIIa–e** were synthesized following the general procedure D by heating 2-(2-thienyl sulfanylmethyl)acrylic acids **VIIa–e** in *N*,*N*-dimethylformamide at 135 °C for 45 min.

**4.7.1. 5,6-Dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid VIIIa.**[20] Compound **VIIIa** was prepared from 2-(2-thienyl sulfanylmethyl)acrylic acid **VIIIa** (0.80 g, 4.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 3% methanol in chloroform) as a white solid (0.73 g, 91%); mp=130–132 °C; [Found: C, 48.17; H, 4.15; S, 31.80. $C_8H_8O_2S_2$ requires: C, 47.98; H, 4.03; S, 32.02]; IR (KBr): 2892, 2601, 1699, 1336, and 1213 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 2.90–3.29 (m, 5H), 6.76 (d, *J* 4.9 Hz, 1H), 7.03 (d, *J* 5.1 Hz, 1H). MS (EI) *m*/*z* 199.0 ($M^{-1}$).

**4.7.2. 2-Methyl-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid VIIIb.** Compound **VIIIb** was prepared from 2-(5-methyl-2-thienyl sulfanylmethyl)acrylic acid **VIIb** (0.85 g, 4.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 3% methanol in chloroform) as a white solid (0.77 g, 90%); mp=126–128 °C; [Found: C, 50.65; H, 4.89; S, 30.13. $C_9H_{10}O_2S_2$ requires: C, 50.44; H, 4.70; S, 29.92]; IR (KBr): 2889, 2611, 1695, 1330, 1225, and 1109 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 2.37 (s, 3H), 2.80–3.03 (m, 2H), 3.13–3.25 (m, 3H), 6.41 (s, 1H). MS (EI) *m*/*z* 213.0 ($M^{-1}$).

**4.7.3. 2-Ethyl-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid VIIIc.** Compound **VIIIc** was prepared from 2-(5-ethyl-2-thienyl sulfanylmethyl)acrylic acid **VIIc** (0.91 g, 4.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 3% methanol in chloroform) as a white solid (0.77 g, 85%); mp=141–143 °C; [Found: C, 52.33; H, 5.05; S, 28.32. $C_{10}H_{12}O_2S_2$ requires: C, 52.60; H, 5.30; S, 28.09]; IR (KBr): 2971, 1698, 1418, 1287, 1209, and 1022 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 1.25 (t, *J* 7.5, 7.5 Hz, 3H), 2.72 (q, *J* 7.1, 6.2, 7.1 Hz, 2H), 2.79–3.02 (m, 2H), 3.07–3.25 (m, 3H), 6.44 (s, 1H). MS (EI) *m*/*z* 227.1 ($M^{-1}$).

**4.7.4. 2-Propyl-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid VIIId.** Compound **VIIId** was prepared from 2-(5-propyl-2-thienyl sulfanylmethyl)acrylic acid **VIId** (0.97 g, 4.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 3% methanol in chloroform) as a white solid (0.83 g, 86%); mp=96–98 °C; [Found: C, 54.27; H, 5.97; S, 26.20. $C_{11}H_{14}O_2S_2$ requires: C, 54.51; H, 5.82; S, 26.46]; IR (KBr): 2876, 1705, 1413, 1269, 1205, and 1022 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 0.95 (t, *J* 7.5, 7.5 Hz, 3H), 1.62 (sextet, *J* 3.0 Hz, 2H), 2.65 (t, *J* 7.5, 7.5 Hz, 2H), 2.86–3.02 (m, 2H), 3.05–3.23 (m, 3H), 6.43 (s, 1H). MS (EI) *m*/*z* 241.1 ($M^{-1}$).

**4.7.5. 2-Cyano-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-5-carboxylic acid VIIIe.** Compound **VIIId** was prepared from 2-(5-cyano-2-thienyl sulfanylmethyl)acrylic acid **VIIe** (0.97 g, 4.0 mmol) in an analogous manner to that for the preparation of **VIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 3% methanol in chloroform) as a white solid (0.85 g, 88%); mp=169–171 °C; [Found: C, 48.10; H, 3.00; N, 6.45; S, 28.27. $C_9H_7NO_2S_2$ requires: C, 47.98; H, 3.13; N, 6.22; S, 28.46]; IR (KBr): 2919, 2213, 1695, 1409, 1279, and 1211 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): $\delta$ 2.90–3.10 (m, 2H), 3.17–3.36 (m, 3H), 7.28 (s, 1H). MS (EI) *m*/*z* 224.0 ($M^{-1}$).

### 4.8. Synthesis of propynyl and acryloyl thioethers of dibenzo[*b*,*d*]furan and dibenzo[*b*,*d*]thiophene Xa,b, XIIa,b

**4.8.1. 4-(2-Propynylsulfanyl)dibenzo[*b*,*d*]furan Xa.** A solution of *n*-butyllithium (4.2 mL of 15% in *n*-hexane, 9.84 mmol) was added to a stirred solution of dibenzofuran (1.5 g, 8.93 mmol) in dry THF (15 mL) at −40 °C over a period of 10 min then stirred at room temperature for 2 h under a nitrogen atmosphere. Reaction was cooled to −40 °C, sulfur (0.286 g, 8.93 mmol) was added and stirring maintained at −40 to −30 °C for 30 min. Then propargyl bromide (1.07 g, 8.99 mmol) was added at the same temperature. The temperature of the reaction was raised to room temperature and stirred for another 30 min. The reaction mixture was slowly quenched with water and extracted with ethyl acetate (2×50 mL). The combined organic layer was washed with water (50 mL) and finally with brine (50 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure to give crude product, which was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 30% chloroform in hexane) to give a white solid (0.51 g, 24%); mp 45–46 °C; [Found: C, 75.38; H, 4.15; S, 13.67. $C_{15}H_{10}OS$ requires: C, 75.60; H, 4.23; S, 13.45]; IR (KBr): 3275, 2955, 1432, 1375, and 1030 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.17 (t, *J* 2.7, 2.7 Hz, 1H), 3.81 (d, *J* 2.4 Hz, 2H), 7.30–7.38 (m, 2H), 7.46 (t, *J* 6.6, 6.6 Hz, 1H), 7.58–7.64 (m, 2H), 7.85–7.95 (m, 2H).

**4.8.2. 4-(2-Propynylsulfanyl)dibenzo[*b*,*d*]thiophene Xb.** Compound **Xb** was prepared from dibenzothiophene (1.64 g, 8.93 mmol) in an analogous manner to that for the preparation of **Xa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 5% ethyl acetate in hexane) as a pale yellow solid (0.68 g, 30%); mp=64–65 °C; [Found: C, 70.69; H, 3.91; S, 25.39. $C_{15}H_{10}S_2$ requires: C, 70.83; H, 3.96; S, 25.21]; IR (KBr): 3283, 2946, 1438, 1384, and 1034 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 2.21 (t, *J* 2.4, 2.4 Hz, 1H), 3.73 (d, *J* 3.0 Hz, 2H), 7.44–7.50 (m, 3H), 7.46 (d, *J* 7.6 Hz, 1H), 7.87–7.90 (m, 1H), 8.10–8.15 (m, 2H).

**4.8.3. 2-Dibenzo[*b*,*d*]furan-4-ylsulfanylmethylacrylic acid XIIa.** A solution of *n*-butyllithium (4.2 mL of 15% in *n*-hexane, 9.84 mmol) was added to a stirred solution of dibenzofuran (1.5 g, 8.93 mmol) in dry THF (15 mL) at −40 °C over a period of 10 min and stirred at room temperature for 2 h under a nitrogen atmosphere. Reaction was cooled to −40 °C, sulfur (0.286 g, 8.93 mmol) was added and stirring maintained at −40 to −30 °C for 30 min. Then a solution of α-(bromomethyl)acrylic acid (0.73 g, 4.47 mmol) in THF (5 mL) and NaOH (0.35 g, 8.95 mmol) in water (5 mL) was added simultaneously over 10 min at the same temperature. The temperature was raised to room temperature and stirred for 30 min. Water (50 mL) was added to the reaction mixture and extracted with ethyl acetate (50 mL). The aqueous layer was acidified with 2 N aq HCl solution, extracted with chloroform (3×50 mL). The combined organic layer was washed with brine (50 mL), dried over sodium sulfate and concentrated to give crude product, which was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 3% methanol in chloroform) to give a white solid (0.46 g, 18%); mp=149–150 °C; [Found: C, 67.48; H, 4.41; S, 11.06. $C_{16}H_{12}O_3S$ requires: C, 67.59; H, 4.25; S, 11.28]; IR (KBr): 2914, 2522, 1698, 1621, 1437, and 1218 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 4.00 (s, 2H), 5.45 (s, 1H), 6.00 (s, 1H), 7.38–7.60 (m, 4H), 7.78 (d, *J* 7.8 Hz, 1H), 8.05 (d, *J* 7.8 Hz, 1H), 8.16 (d, *J* 7.8 Hz, 1H) 12.80 (hump, 1H).

**4.8.4. 2-Dibenzo[*b*,*d*]thiophene-4-ylsulfanylmethylacrylic acid XIIb.** Compound **XIIb** was prepared from dibenzothiophene (1.0 g, 5.43 mmol) in an analogous manner to that for the preparation of **XIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (0.41 g, 25%); mp=162–165 °C; [Found: C, 63.72; H, 4.21; S, 21.45. $C_{16}H_{12}O_2S_2$ requires: C, 63.97; H, 4.03; S, 21.35]; IR (KBr): 2916, 1696, 1438, 1309, and 1213 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 3.94 (s, 2H), 5.48 (d, *J* 0.9 Hz, 1H), 5.94 (d, *J* 1.2 Hz, 1H), 7.51–7.60 (m, 4H), 8.06 (d, *J* 7.5 Hz, 1H), 8.30 (d, *J* 8.7 Hz, 1H), 8.35 (d, *J* 7.8 Hz, 1H), 12.80 (hump, 1H).

**4.8.5. 2*H*-Benzo[*b*]thiochromeno[7,8-*d*]furan XIa.** Compound **XIa** is synthesized following the procedure B by heating 4-(2-propynylsulfanyl)dibenzo[*b*,*d*]furan **Xa** (0.95 g, 4.0 mmol) in *N*,*N*-diethylaniline at 220 °C for 8 h under nitrogen atmosphere. The crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 15% chloroform in hexane) as a white solid (0.52 g, 55%); mp=95–97 °C; [Found: C, 75.88; H, 4.13; S, 13.64. $C_{15}H_{10}OS$ requires: C, 75.60; H, 4.23; S, 13.45]; IR (KBr): 2884, 1450, 1407, 1201, 1185, and 1019 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): δ 3.55 (dd, *J* 1.5, 1.5 Hz, 2H), 5.97 (q, *J* 5.4, 4.2, 5.4 Hz, 1H), 6.65 (d, *J* 10.5 Hz, 1H), 7.05 (d, *J* 7.8 Hz, 1H), 7.31 (t, *J* 6.6, 6.6 Hz, 1H), 7.43 (t, *J* 7.3, 7.3 Hz, 1H), 7.68 (d, *J* 9.3 Hz, 1H), 7.71 (d, *J* 7.8 Hz, 1H), 7.86 (d, *J* 8.1 Hz, 1H). MS (EI) *m*/*z* 237.3 ($M^{-1}$).

**4.8.6. 2*H*-Benzo[*b*]thiochromeno[7,8-*d*]thiophene XIb.** Compound **XIb** was prepared from 4-(2-propynylsulfanyl)-dibenzo[*b*,*d*]thiophene **Xb** (0.95 g, 4.0 mmol) in an analogous manner to that for the preparation of **XIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 15% chloroform in hexane) as a gummy oil (1.0 g, 70%); [Found: C, 70.93; H, 3.84; S, 25.38. $C_{15}H_{10}S_2$ requires: C, 70.83; H, 3.96; S, 25.21]; IR (neat): 3033, 1446, 1366, 1115, 1038, and 832 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): δ 3.62 (dd, *J* 1.5, 1.5 Hz, 2H), 6.01 (q, *J* 5.5, 4.0, 5.5 Hz, 1H), 6.66 (dt, *J* 3.5, 2.6 Hz, 1H), 7.18 (d, *J* 7.8 Hz, 1H), 7.43–7.46 (m, 2H), 7.85–7.89 (m, 2H), 9.10 (d, *J* 8.8 Hz, 1H). MS (EI) *m*/*z* 253.2 ($M^{-1}$).

**4.8.7. 3,4-Dihydro-2*H*-benzo[*b*]thiochromeno[7,8-*d*]-furan-3-carboxylic acid XIIIa.** Compound **XIIIa** is synthesized following the procedure D by heating 2-dibenzo[*b*,*d*]furan-4-ylsulfanylmethylacrylic acid **XIIa** (1.1 g, 4.0 mmol) in *N*,*N*-dimethylformamide at 150 °C for 5 h under a nitrogen atmosphere. The crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (0.72 g, 65%); mp=253–254 °C; [Found: C, 67.75; H, 4.13; S, 11.40. $C_{16}H_{12}O_3S$ requires: C, 67.59; H, 4.25; S, 11.28]; IR (KBr): 2885, 2603, 1694, 1409, 1192, 1152, and 938 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 3.28–3.74 (m, 5H), 7.21 (d, *J* 7.8 Hz, 1H), 7.39 (t, *J* 7.2, 7.2 Hz, 1H), 7.50 (t, *J* 7.2, 7.2 Hz, 1H), 7.76 (t, *J* 8.1, 8.1 Hz, 2H), 8.09 (d, *J* 7.5 Hz, 1H), 12.75 (hump, 1H). MS (EI) *m*/*z* 283.1 ($M^{-1}$).

**4.8.8. 3,4-Dihydro-2*H*-benzo[4,5]thieno[3,2-*h*]thiochromene-3-carboxylic acid XIIIb.** Compound **XIIIb** was prepared from 2-dibenzo[*b*,*d*]thiophene-4-ylsulfanylmethylacrylic acid **XIIb** (1.2 g, 4.0 mmol) in an analogous manner to that for the preparation of **XIIIa**, and the crude product obtained was purified by column chromatography (stationary phase: silica gel 60–120, mobile phase: 2% methanol in chloroform) as a white solid (0.888 g, 74%); mp=254–256 °C; [Found: C, 64.17; H, 3.97; S, 21.56. $C_{16}H_{12}O_2S_2$ requires: C, 63.97; H, 4.03; S, 21.35]; IR (KBr): 2888, 1697, 1406, 1271, and 1192 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$): δ 3.09–3.45 (m, 5H), 7.33 (d, *J* 8.4 Hz, 1H), 7.51 (m, 2H), 8.03 (d, *J* 7.8 Hz, 2H), 8.13 (d, *J* 7.8 Hz, 1H), 12.75 (hump, 1H). MS (EI) *m*/*z* 299.1 ($M^{-1}$).

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