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P_4S_{10} and Na_2S-mediated novel annulation routes to *c*-fused thiophenes†

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Two efficient hetero-annulation protocols have been developed for the synthesis of stable substituted *c*-fused thiophene derivatives with moderate to high yield. 3-(2-formyl-phenyl)-acrylic acid esters afforded benzo[*c*]thiophenes in the presence of phosphorus pentasulfide in refluxing benzene while 3-(2-formyl-cycloalkenyl)α,β-unsaturated esters resulted in the formation of *c*-fused thiophene derivatives when reacted with sodium sulfide in refluxing tetrahydrofuran.

Introduction

Thiophene derivatives have gained a potential position in the heterocyclic family because of their diverse biological,[1] pharmacological,[2] material,[3] and synthetic applications.[4] Benzothiophenes are one of the most important members of this thiophene family. Several synthetic routes and potential applications are available for benzo[*b*]thiophenes.[5,6] Benzo[*c*]thiophenes are also important in terms of biological[7] as well as material properties.[8] Some hydrogenated benzo[*c*]thiophene derivatives, those act as agonists for the G protein-coupled receptor S1P1/EDG1 and have a powerful, long lasting immunosuppressive effect, are useful to treat uncontrolled inflammatory disease and improve vascular functionality.[7]

1,3-Diaryl-benzo[*c*]thiophenes (**1**) shows interesting electronic and optical properties[8] while compound **2** have potential application in OLEDs (Fig. 1).[9]

Several synthetic routes were targeted towards the synthesis of benzo[*c*]thiophene skeletons. Cava *et al.* reported synthesis of benzo[*c*]thiophene applying Pummerer-type dehydration strategy.[10] Musmanni and Ferraris reported P_2S_5 mediated synthesis of 1,3-di-(2-thienyl)-benzo[*c*]thiophenes and conducting polymers based on it.[11] Kiebooms and co-workers synthesized 1,3-dithienylisothianaphthenes from *ortho* dicarboxylic arene derivatives *via* Grignard reaction.[12]

Mohanakrishnan and Amaladass reported synthesis of 1,3-diaryl benzo[*c*]thiophenes from lactones using Lawesson's reagent.[13] Our objective was to synthesize benzo[*c*]thiophene skeleton using shorter and high-yielding synthetic strategy.

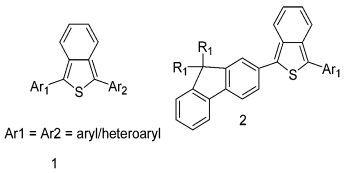
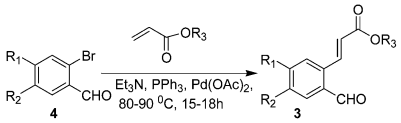


Fig. 1 Benzo[c]thiophenes with important electronic and material properties.

Results and discussion

A previous report from our group described efficient synthesis of benz[*e*]indene derivatives from 3-(2-formyl-cycloalkenyl)-acrylic acid esters using diphosphorus pentasulfide (P_4S_{10}) at room temperature.[14] We initially attempted to synthesize thiophene derivatives using P_4S_{10} but interestingly we ended up with indene derivatives. In continuation to that work, we carried out the same experiment with the aromatic analogues of the acrylic acid esters {3-(2-formyl-phenyl)-acrylic acid esters} (**3**) which were not dealt with in the previous report. The starting materials **3** were synthesized in good yields from 2-bromocarboxaldehydes (**4**) by Heck reaction using acrylate esters in presence of palladium acetate {$Pd(OAc)_2$}, triethylamine (Et_3N), and triphenylphosphine (PPh_3) at 80–90 °C for 15–18 h (Scheme 1).[15]

3a (1 mmol) was initially reacted with P_4S_{10} (1.5 mmol) in benzene (4 mL) under argon at rt for 12 h to give benzo[*c*]thiophene-1-yl-acetic acid ethyl ester **5a** in 75% yield (Table 1, entry 1). When the same reaction was carried out in air, yield of the product **5a** was very low (30%). Next, we performed the reaction by refluxing in benzene. All the starting material was consumed



Scheme 1 Synthesis of 3-(2-formyl-phenyl)-acrylic acid esters **3**.

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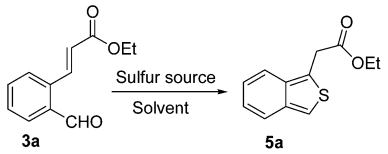
† Electronic supplementary information (ESI) available. CCDC 984824. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ra01639d

Table 1 Optimization studies[a,b]



Entry	Sulfur source	Solvent	Temperature (°C)	Time (h)	Yield[c] (%)
1	P_4S_{10}	Benzene	RT	12	75
2	P_4S_{10}	Benzene	85	8	77
3	P_4S_{10}	DCM	45	16	35
4	LR	Benzene	85	20	10
5	Na_2S	THF	70	8	Decomposed mixture

[a] Reagents and conditions: **3a** (1 mmol), P_4S_{10} (1.5 mmol), and solvent (4 mL). [b] Reaction was done in a two-necked round-bottomed flask fitted with a condenser under argon. [c] Yields refer to the isolated yields after purification through column chromatography.

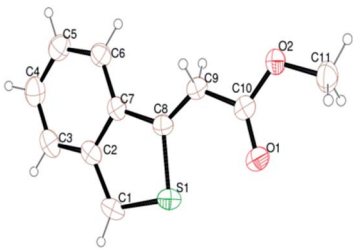


Fig. 2 ORTEP view of **5d**.

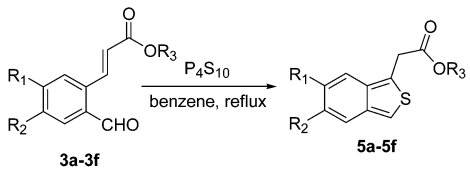
after 8 h to give **5a** in 77% yield. Lawesson's reagent (LR) also gave the desired product but the yield was too low (Table 1, entry 4). Na_2S led to a mixture of decomposed products. The desired product was also obtained with P_4S_{10} in CH_2Cl_2 (DCM) but with a low product yield. After screening through three sulfur sources (Table 1), the reaction was found to be most effective with P_4S_{10} in refluxing benzene (Table 1, entry 2). The reaction was incomplete with <1.5 equiv. of P_4S_{10}.

The product structure was confirmed by single-crystal-X-ray diffraction. An ORTEP drawing of **5d** with the atom numbering is shown in Fig. 2.

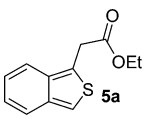
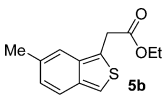
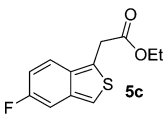
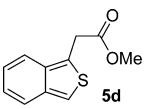
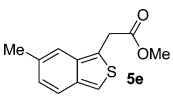
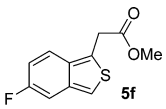
Having established the exact structure and the optimal conditions, we next tried to generalize our methodology. We obtained benzo[*c*]thiophene-1-yl-acetic acid esters (**5a–f**) in good yields (Table 2).

As a course of mechanistic explanation, it can be postulated that initially a thio-aldehyde **6** is formed as a reactive intermediate which undergoes immediate intramolecular cyclization by 1,4-addition to form intermediate **7**. **7** loses proton to give thiophene derivative **8** which finally tautomerizes to the desired product **5** (Scheme 2). Formation of thioaldehyde intermediate **6** is presumed, based on the reported synthesis of thione from α,β-unsaturated ketone in presence of Lawesson's reagent which behaves analogously as P_4S_{10}.[16]

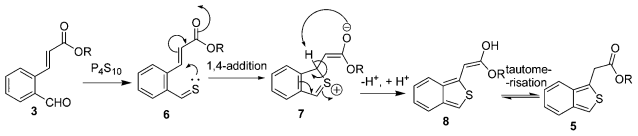
Table 2 Synthesis of benzo[*c*]thiophene-1-yl-acetic acid esters[a]



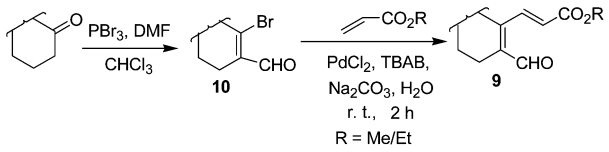
R_1 = H, Me; R_2 = H, F; R_3 = Me, Et

Entry	R_1	R_2	R_3	Time (h)	Product	Yield[b] (%)
1	H	H	Et	8	 **5a**	77
2	Me	H	Et	10	 **5b**	72
3	H	F	Et	8	 **5c**	76
4	H	H	Me	8	 **5d**	75
5	Me	H	Me	10	 **5e**	66
6	H	F	Me	9	 **5f**	71

[a] Reagents and conditions: all the reactions were carried out under the following conditions: substrates **3a–f** (1 mmol), P_4S_{10} (1.5 mmol), and benzene (4 mL) at 85 °C under argon. [b] Yields were determined after purification through column chromatography.



Scheme 2 Plausible rationale for the formation of benzo[*c*]thiophene-1-yl-acetic acid esters **5**.

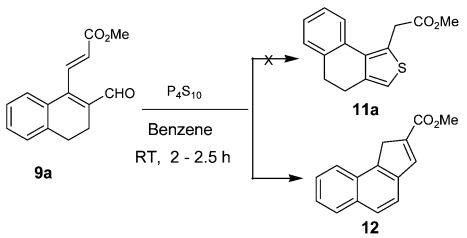


Scheme 3 Palladium catalyzed synthesis of precursor **9**.

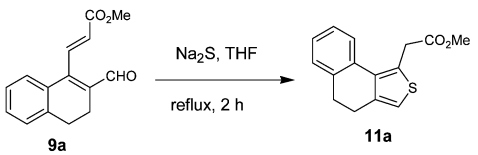
After successful synthesis of benzo[*c*]thiophene derivatives from the aromatic analogues of the acrylic acid esters, once again we directed our focus to develop a general, simple and effective method for the preparation of *c*-fused thiophene derivatives from 3-(2-formyl-cycloalkenyl)α,β-unsaturated esters **9** with which we have already reported the synthesis of furan, dihydrofuran, pyrrole, benz[*e*]indene and cyclopentanone derivatives.[14,17]

The starting materials 3-(2-formyl-cycloalkenyl)α,β-unsaturated esters **9** were synthesized in good yields (90–99%) by reported procedure[17] where β-bromovinyl aldehydes **10** were treated with acrylate esters in the presence of palladium chloride, sodium carbonate and tetrabutylammonium bromide in water at room temperature for 2–3 h (Scheme 3) thereby, producing Pd(0) nanoparticles *in situ*.[18]

The preliminary experiment with the model substrate 3-(2-formyl-3,4-dihydro-naphthalen-1-yl)-acrylic acid ester **9a** and phosphorus pentasulphide in benzene solvent, instead of giving thiophene derivative **11a**, unexpectedly afforded benz[*e*]indene derivative **12** (Scheme 4), which has already been discussed in our previous communication.[14]



Scheme 4 Synthesis of benz[*e*]indene.

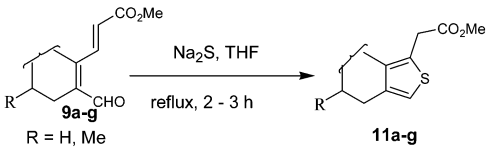


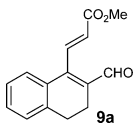
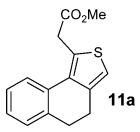
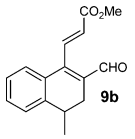
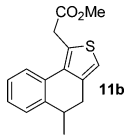
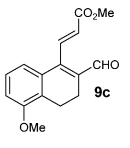
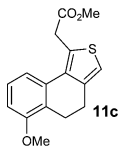
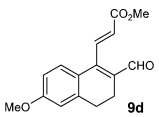
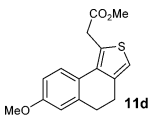
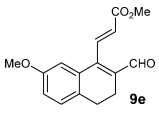
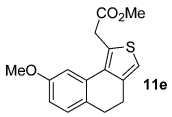
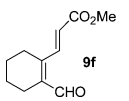
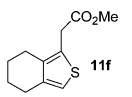
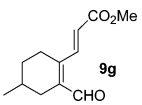
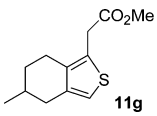
Scheme 5 Synthesis of thiophene **11a** with Na_2S.

Then the precursor **9a** was treated with Na_2S at room temperature but no reaction occurred and the starting material was recovered. We then thought of making reaction condition more drastic *i.e.* increasing the reaction temperature. Na_2S was employed as the source of sulfur for this purpose. We avoided LR because it behaves analogously as that of P_4S_{10} which leads to benz[*e*]indenes. When the precursor **9a** was treated with Na_2S in THF solvent at refluxing condition for 2 h, we were delighted to obtain our desired thiophene **11a** (Scheme 5). After a quick optimization of the reactant ratio (**9a**/Na_2S = 1.0 : 1.5), the yield of product **11a** was increased to 80%.

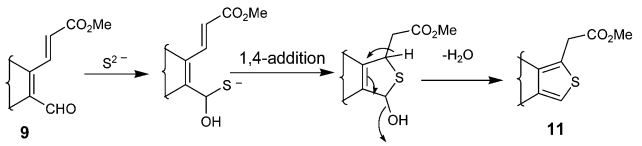
With the optimized reaction condition in hand, we next examined the generality and substrate scope of this new cyclization reaction. We have synthesized and characterized

Table 3 Synthesis of thiophene derivatives[a]



Entry	Formyl-alkene **9**	Thiophene **11**	Time (h)	Yield[b] (%)
1			2	80
2			2.5	75
3			2.5	77
4			3.0	70
5			3.0	75
6			2	55
7			2	52

[a] Reaction was carried out with formyl-alkene **9** (1.0 mmol) and Na_2S (1.5 mmol) in THF at refluxing condition for 2–3 h. [b] Isolated yields after purification by column chromatography.



Scheme 6 Plausible mechanism of thiophene synthesis.

some *c*-fused thiophene derivatives **11a–g** by this one pot reaction (Table 3). Relatively lower yields were obtained with 3-(2-formylcyclohexenyl)-acrylic acid esters (Table 3, entries 6 and 7). Moderate to good yields were achieved with esters of 3-(2-formyl-3,4-dihydro-naphthalen-1-yl)-acrylic acid.

Mechanistically we believe that these reactions are proceeding in a similar fashion to that of the pyrrole synthesis described previously.[17b] The attack of the sulfide on the aldehyde followed by intra-molecular 1,4-addition and subsequent elimination of water leads to the thiophene derivatives **11** (Scheme 6). Aromaticity provides the impetus for this type of cyclization.

Conclusions

We have demonstrated the successful preparation of substituted *c*-fused thiophene derivatives starting from 3-(2-formyl-phenyl)-acrylic acid esters and 3-(2-formyl-cycloalkenyl)-acrylic esters. The aromatic precursors required P_4S_{10} as the annulation reagent while the other substrates were effective in presence of Na_2S. The developed one-pot methodologies are clean and free from side-products. Furthermore, the reagents systems used are safe, simple and inexpensive.

Experimental section

General remarks

All reactions were carried out using oven-dried glassware. Commercial grade reagents were used without further purification. Solvents were dried and distilled following usual protocols prior to use. All yields refer to isolated yields after column purification. Column chromatography was carried out using Silica gel (60–120 mesh) purchased from Rankem, India. TLC was performed on aluminium-backed plates coated with Silica gel 60 with F254 indicator (Merck).

The ^{1}H NMR spectra were measured with Bruker-200 (200 MHz) or Bruker-400 (400 MHz) and ^{13}C NMR spectra were measured with Bruker-200 (50 MHz) or Bruker-400 (100 MHz) using $CDCl_3$. Coupling constants in ^{1}H NMR are in Hz. TOF MS ES$^+$ spectra were recorded using XEVO-G2QTOF-YCA288 or Qtof Micro YA263. Melting points were measured in Toshniwal (India) melting point apparatus.

General procedure for the synthesis of 3-(2-formyl-phenyl)-acrylic acid esters (3a–f)

To a solution of 2-bromocarboxaldehyde (1 mmol) in Et_3N (5 mL), methyl/ethyl acrylate (1.5 mmol), PPh_3 (0.25 mmol) and $Pd(OAc)_2$ (10 mol%) were added and heated at 80–90 °C for 15–18 h. The reaction mixture was cooled to rt and extracted with EtOAc (3 × 20 mL). Combined organic layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the crude product was purified through column chromatography using silica gel (60–120 mesh) and pet. ether–EtOAc as eluent.

General procedure for the preparation of benzo[*c*]thiophene-1-yl-acetic acid esters (5a–f)

To a solution of 3-(2-formyl-phenyl)-acrylic acid ester (1.0 mmol) in benzene (4 mL), P_4S_{10} (1.5 mmol) was added and refluxed for 8–10 h under argon atmosphere. After evaporating the solvent from the reaction mixture, the crude was directly used for purification through column chromatography using ethyl acetate–petroleum ether as eluent.

General procedure for Heck reaction in water

β-Bromovinyl aldehyde (1 mmol), Na_2CO_3 (4 mmol), Bu_4NBr (1 mmol), $PdCl_2$ (10 mol%) and water (5 mL) were placed in a two neck round bottom flask. To the mixture methyl acrylate (4 mmol) was added, stirred for 2 h, diluted with aqueous NH_4Cl solution and extracted with ether (3 × 25 mL). The organic layers were combined, washed with brine, dried over Na_2SO_4 and then concentrated. The product was purified by column chromatography using ethyl acetate–petroleum ether as eluent.

General procedure for the preparation of thiophenes 11

To a solution of 3-(2-formyl-cycloalkenyl)-acrylic acid ester (1.0 mmol) in dry THF (5 mL), Na_2S (1.5 mmol) was added and refluxed for 2–3 h. After evaporating the solvent of the reaction mixture, 50 mL diethyl ether was added to it, washed with brine solution, dried over Na_2SO_4 and then concentrated. The product was purified by column chromatography using ethyl acetate–petroleum ether as eluent.

Spectral and analytical data of compounds

Compounds **3a**,[19] **3b**,[15] **3c**,[20] **3d**,[21] **3e**,[22] **3f** (ref. 23) are previously reported.

Benzo[*c*]thiophen-1-yl-acetic acid ethyl ester (5a). Yellow solid. M. P. 96 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.33$ (t, $J = 7.2$ Hz, 3H), 4.27 (q, $J = 7.2$ Hz, 2H), 4.37 (s, 2H), 6.49 (s, 1H), 7.33–7.44 (m, 3H), 7.70 (d, $J = 7.0$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 14.67$, 38.85, 60.29, 102.42, 121.92, 125.65, 127.66, 130.58, 138.13, 143.88, 163.52, 168.21. HRMS calcd for $C_{12}H_{13}O_2S$ $(M + H)^+$ $m/z = 221.0636$, found $m/z = 221.0667$. Anal. calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found C, 65.69; H, 5.25.

6-Methyl-benzo[*c*]thiophen-1-yl-acetic acid ethyl ester (5b). Reddish yellow solid. M. P. 82 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.37$ (t, $J = 7.0$ Hz, 3H), 2.45 (s, 3H), 4.31 (q, $J = 7.0$ Hz, 2H), 4.37 (s, 2H), 6.51 (s, 1H), 7.26–7.38 (m, 2H), 7.54 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 14.70$, 21.40, 38.57, 60.27, 102.20, 122.22, 125.31, 131.82, 137.58, 138.32, 141.23, 163.69, 168.33. Anal. calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found C, 66.49; H, 6.35.

5-Fluoro-benzo[*c*]thiophen-1-yl-acetic acid ethyl ester (5c). Yellow solid. M. P. 118 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.33 (t, J = 7.2 Hz, 3H), 4.27 (q, J = 7.2 Hz, 2H), 4.36 (s, 2H), 6.41 (s, 1H), 7.04–7.14 (m, 2H), 7.63–7.70 (m, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.68, 38.51 (d), 60.40, 102.34, 112.54 (d), 115.65 (d), 123.35 (d), 134.36, 146.18 (d), 162.03 (d), 166.99, 168.16. Anal. calcd for $C_{12}H_{11}FO_2S$: C, 60.49; H, 4.65. Found C, 60.27; H, 6.91.

Benzo[*c*]thiophen-1-yl-acetic acid methyl ester (5d). Brown solid. M. P. 109 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.81 (s, 3H), 4.39 (s, 2H), 6.50 (s, 1H), 7.34–7.46 (m, 3H), 7.71 (d, J = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 38.89, 51.58, 101.95, 121.98, 125.70, 127.71, 130.68, 138.08, 143.97, 163.92, 168.67. HRMS calcd for $C_{11}H_{11}O_2S$ (M + H)$^+$ m/z = 207.0480, found m/z = 207.0502. Anal. calcd for $C_{11}H_{10}O_2S$: C, 64.05; H, 4.89. Found C, 64.39; H, 6.65.

6-Methyl-benzo[*c*]thiophen-1-yl-acetic acid methyl ester (5e). Brown solid. M. P. 96 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.42 (s, 3H), 3.80 (s, 3H), 4.33 (s, 2H), 6.47 (s, 1H), 7.23–7.35 (m, 2H), 7.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.40, 38.57, 51.55, 101.68, 122.20, 125.32, 131.88, 137.60, 138.24, 141.28, 164.07, 168.73. HRMS calcd for $C_{12}H_{13}O_2S$ (M + H)$^+$ m/z = 221.0636, found m/z = 221.0697. Anal. calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found C, 65.04; H, 5.77.

5-Fluoro-benzo[*c*]thiophen-1-yl-acetic acid methyl ester (5f). Reddish yellow solid. M. P. 126 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.80 (s, 3H), 4.36 (s, 2H), 6.41 (s, 1H), 7.05–7.14 (m, 2H), 7.63–7.73 (m, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 38.51 (d), 31.62, 101.83, 112.55 (d), 115.65 (d), 123.37 (d), 134.31 (d), 146.25 (d), 162.23 (d), 167.02, 168.56. HRMS calcd for $C_{11}H_{10}FO_2S$ (M + H)$^+$ m/z = 225.0386, found m/z = 225.0414. Anal. calcd for $C_{11}H_9FO_2S$: C, 58.92; H, 4.05. Found C, 58.67; H, 4.41.

3-(2-Formyl-3,4-dihydro-naphthalen-1-yl)-acrylic acid methyl ester (9a). Yellow liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.50–2.54 (m, 2H), 2.65–2.73 (m, 2H), 3.75 (s, 3H), 6.11 (d, J = 15.8 Hz, 1H), 7.12–7.30 (m, 4H), 7.76 (dd, J_1 = 1.2 Hz, J_2 = 16.0 Hz, 1H), 9.99 (d, J = 0.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.34, 27.08, 51.84, 126.62, 126.73, 128.02, 128.41, 130.48, 132.45, 136.64, 138.19, 138.25, 147.37, 165.48, 190.58. HRMS calcd for $C_{15}H_{14}O_3Na$ (M + Na)$^+$ m/z = 265.0841, found m/z = 265.0845. Anal. calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found C, 74.02; H, 6.10.

3-(2-Formyl-4-methyl-3,4-dihydro-naphthalen-1-yl)-acrylic acid methyl ester (9b). Yellow semi solid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.19 (d, J = 6.8 Hz, 3H), 2.39–2.69 (m, 2H), 2.86–2.97 (m, 1H), 3.80 (s, 3H), 6.16 (d, J = 15.8 Hz, 1H), 7.20–7.36 (m, 4H), 7.83 (d, J = 15.8 Hz, 1H), 10.06 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 19.48, 27.98, 31.40, 52.01, 126.67, 126.72, 126.99, 128.58, 131.01, 131.77, 135.47, 138.44, 143.29, 147.16, 165.67, 191.07. Anal. calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found C, 74.83; H, 6.45.

3-(2-Formyl-5-methoxy-3,4-dihydro-naphthalen-1-yl)-acrylic acid methyl ester (9c). Yellow semi solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.56 (t, J = 8.0 Hz, 2H), 2.80 (t, J = 8.0 Hz, 2H), 3.83 (s, 3H), 3.85 (s, 3H), 6.17 (d, J = 16.0 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.82 (d, J = 16.0 Hz, 1H), 10.07 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 19.53, 20.12, 52.22, 55.86, 113.20, 119.44, 126.78, 127.23, 128.66, 133.76, 137.12, 138.96, 147.92, 156.55, 165.96, 191.31. Anal. calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found C, 70.73; H, 5.81.

3-(2-Formyl-6-methoxy-3,4-dihydro-naphthalen-1-yl)-acrylic acid methyl ester (9d). Yellow semi-solid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.56–2.64 (m, 2H), 2.74–2.81 (m, 2H), 3.84 (s, 6H), 6.18 (d, J = 15.8 Hz, 1H), 6.73–6.78 (m, 2H), 7.28–7.33 (m, 1H), 7.82 (d, J = 15.8 Hz, 1H), 10.06 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.60, 28.06, 52.27, 55.62, 112.14, 114.26, 125.70, 128.62, 128.83, 134.88, 138.99, 141.00, 148.13, 161.78, 166.03, 190.95. Anal. calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found C, 70.29; H, 6.24.

3-(2-Formyl-7-methoxy-3,4-dihydro-naphthalen-1-yl)-acrylic acid methyl ester (9e). Yellow semi-solid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.52–2.59 (m, 2H), 2.66–2.74 (m, 2H), 3.76 (s, 3H), 3.81 (s, 3H), 6.16 (d, J = 15.8 Hz, 1H), 6.81–6.87 (m, 2H), 7.13 (d, J = 8.6Hz, 1H), 7.78 (td, J_1 = 1.4 Hz, J_2 = 15.8 Hz, 1H), 10.05 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.99, 26.45, 52.13, 55.60, 113.09, 115.52, 128.78, 128.95, 130.52, 133.61, 137.36, 138.43, 147.72, 158.54, 165.76, 191.09. Anal. calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found C, 70.33; H, 6.16.

3-(2-Formyl-cyclohex-1-enyl)-acrylic acid methyl ester (9f). Yellow liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.49–1.55 (m, 4H), 2.18–2.29 (m, 4H), 3.63 (s, 3H), 6.00 (d, J = 15.6 Hz, 1H), 8.16 (d, J = 15.6 Hz, 1H), 10.27 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.92, 21.39, 23.26, 26.67, 51.68, 121.50, 138.21, 140.42, 147.64, 166.61, 189.65. Anal. calcd for $C_{11}H_{14}O_3$ (194.0943): C, 68.02; H, 7.27. Found C, 68.20; H, 7.17.

3-(2-Formyl-4-methyl-cyclohex-1-enyl)-acrylic acid methyl ester (9g). Yellow liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.95 (d, J = 8 Hz, 3H), 1.65–1.85 (m, 4H), 2.28–2.63 (m, 3H), 3.76 (s, 3H), 6.12 (d, J = 15.6 Hz, 1H), 8.27 (d, J = 15.6 Hz, 1H), 10.39 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.50, 27.22, 27.54, 29.80, 31.81, 52.07, 122.02, 138.39, 140.38, 147.71, 167.01, 189.49. Anal. calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found C, 69.40; H, 7.57.

(4,5-Dihydro-naphtho[1,2-*c*]thiophen-1-yl)-acetic acid methyl ester (11a). Red liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.74–2.87 (m, 4H), 3.77 (s, 3H), 4.07 (s, 2H), 6.90 (s, 1H), 7.19–7.34 (m, 3H), 7.60 (d, J = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 26.52, 31.14, 35.37, 52.60, 116.95, 125.56, 127.05, 127.12, 128.73, 129.06, 132.63, 134.85, 138.32, 140.50, 171.24. HRMS calcd for $C_{15}H_{14}O_2SNa$ (M + Na)$^+$ m/z = 281.0612, found m/z = 281.0615. Anal. calcd for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46; found C, 69.49; H, 5.59.

(5-Methyl-4,5-dihydro-naphtho[1,2-*c*]thiophen-1-yl)-acetic acid methyl ester (11b). Red liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.16 (d, J = 6.8 Hz, 3H), 2.62 (dd, J_1 = 6.0 Hz, J_2 = 15.6 Hz, 1H), 2.88 (dd, J_1 = 4.6 Hz, J_2 = 15.4 Hz, 1H), 2.97–3.09 (m, 1H), 3.77 (s, 3H), 4.08 (d, J = 1.4 Hz, 2H), 6.91 (s, 1H), 7.24–7.35 (m, 3H), 7.61 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 20.20, 33.89, 35.16, 35.46, 52.68, 117.84, 125.76, 126.97, 127.40, 127.43, 128.91, 131.82, 134.33, 139.08, 142.97, 171.34. Anal. calcd for $C_{16}H_{16}O_2S$: C, 70,56; H, 5.92; found C, 70.42; H, 6.03.

(6-Methoxy-4,5-dihydro-naphtho[1,2-*c*]thiophen-1-yl)-acetic acid methyl ester (11c). Red liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.60–2.67 (m, 2H), 2.82–2.91 (m, 2H), 3.75 (s, 3H), 3.85 (s, 3H), 3.92 (s, 2H), 6.82 (s, 1H), 7.11–7.24 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.56, 21.82, 34.15, 52.39, 55.48, 108.73, 116.71, 117.98, 122.98, 125.14, 127.03, 130.57, 135.27, 141.80, 156.89,

169.86. HRMS calcd for $C_{16}H_{17}O_3S$ $(M + H)^+$ $m/z = 289.0898$, found $m/z = 289.0907$. Anal. calcd for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59; found C, 66.51; H, 5.79.

(7-Methoxy-4,5-dihydro-naphtho[1,2-*c*]thiophen-1-yl)-acetic acid methyl ester (11d). Brown liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.78$ (bs, 4H), 3.77 (s, 3H), 3.83 (s, 3H), 4.03 (s, 2H), 6.78–6.88 (m, 3H), 7.56 (d, $J = 7.8$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 26.58$, 31.55, 35.41, 52.61, 55.48, 112.14, 114.49, 116.88, 125.79, 126.78, 127.25, 134.73, 140.12, 140.16, 158.70, 171.37. Anal. calcd for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59; found C, 66.45; H, 5.91.

(8-Methoxy-4,5-dihydro-naphtho[1,2-*c*]thiophen-1-yl)-acetic acid methyl ester (11e). Brown liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.80$ (bs, 4H), 3.82 (s, 3H), 3.90 (s, 3H), 4.11 (s, 2H), 6.83 (dd, $J_1 = 2.6$ Hz, $J_2 = 8.4$ Hz, 1H), 6.94 (s, 1H), 7.21–7.29 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 26.63$, 30.01, 35.22, 52.42, 55.42, 110.93, 112.77, 116.78, 128.90, 129.22, 130.31, 133.22, 134.82, 140.45, 158.55, 171.01. Anal. calcd for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59; found C, 66.31; H, 5.82.

(4,5,6,7-Tetrahydro-benzo[*c*]thiophen-1-yl)-acetic acid methyl ester (11f). Yellow liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.69$–1.75 (m, 4H), 2.55–2.71 (m, 4H), 3.70 (s, 2H), 3.71 (s, 3H), 6.76 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 23.23$ (2C), 24.73, 26.47, 33.26, 52.15, 117.48, 127.31, 136.12, 138.69, 170.94. HRMS calcd for $C_{11}H_{15}O_2S$ $(M + H)^+$ $m/z = 211.0793$, found $m/z = 211.0803$. Anal. calcd for $C_{11}H_{14}O_2S$: C, 62.83; H, 6.71. Found C, 62.65; H, 6.82.

(5-Methyl-4,5,6,7-tetrahydro-benzo[*c*]thiophen-1-yl)-acetic acid methyl ester (11g). Yellow liquid. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.04$ (d, $J = 8.0$ Hz, 3H), 1.30–1.42 (m, 1H), 1.69–1.92 (m, 2H), 2.14–2.27 (m, 1H), 2.39–2.56 (m, 1H), 2.67–2.86 (m, 2H), 3.70 (s, 2H), 3.71 (s, 3H), 6.74 (s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 21.54$, 24.18, 29.48, 31.52, 33.34, 34.94, 52.15, 117.25, 127.13, 135.88, 139.04, 170.94. Anal. calcd for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19; found C, 64.42; H, 7.03.

Crystallographic parameters of compound **5d**:

Compound	**5d**
CCDC number	984824
Empirical formula	$C_{11}H_{10}O_2S$
Formula weight	206.25
Temperature	293 (2) K
Crystal system	Orthorhombic
Space group	*P*2(1)2(1)2(1)
a	5.361 (5) Å
b	11.911 (5) Å
c	15.763 (5) Å
α	90.000 (5)
β	90.000 (5)
γ	90.000 (5)
Volume	1006.5 (11) Å^3
Z	4
Calculated density	1.361 Mg m^{-3}
Absorption coefficient	0.290 mm^{-1}
F(000)	432
Crystal size	0.15 × 0.14 × 0.11 mm^3
Theta range for data collection	2.14 to 24.99°
Goodness-of-fit on F^2	1.074
Final *R* indices [$I > 2$sigma (I)]	$R_1 = 0.0490$, w$R_2 = 0.1460$

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