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α-Oxoketene Dithioacetals Mediated Benzoannelation of Aromatic Heterocycles: an Efficient Regiocontrolled Synthesis of Highly Substituted and Polycyclic Benzo[*b*]thiophenes

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Abstract—An efficient regiocontrolled synthesis of highly substituted and complex polycyclic benzo[*b*]thiophenes has been developed via our benzoannelation strategy involving conjugate addition–displacement on a variety of α-oxoketene dithioacetals by carbanions derived from 2- and 3-cyanomethylthiophenes followed by acid induced cyclization of the resulting conjugate adducts.

Introduction

The chemistry of benzo[*b*]thiophenes received its early stimulus from the discovery of thioindigo dyes introduced in 1906.[1] They are also found to be clinically useful as antihistamines, cardiac drugs possessing vasopressure activity and their biosteric relationship with indoles has yielded many benzothiophenes with interesting pharmacological properties.[2] Thus the benzothiophene ring system may replace benzene, naphthalene or indole rings to produce biologically active molecules with different physiological disposition, metabolism and lower toxicity.[3]

Benzothiophenes are generally synthesised by the construction of a thiophene component onto a thiophenol precursor.[4–6] Subsequently a number of approaches for benzo[*b*]thiophene synthesis involving annelation of a benzene ring on a preformed thiophene moiety were developed.[7–30] Various approaches for benzologation of thiophene described in the literature involve: (a) side chain elaboration of substituted thiophenes either through the Stobbe cyclization or via acid catalysed cyclization of a β-ketosulfoxide;[7–13] (b) Michael addition and intramolecular cyclization of *ortho* substituted thiophenes bearing electrophilic and potentially nucleophilic carbon substituents;[14] (c) Diels–Alder reaction of vinyl thiophenes;[15–17] (d) [4+2] cycloaddition of thieno-2,3-*o*-xylylenes and their heterocyclic analogs such as thieno[2,3-*c*]furan, thieno[2,3-*c*]pyrrole and thieno[2,3-*c*]pyranone;[18–25] (e) Pd catalysed cyclocarbonylation of 2- and 3-thienyl allylic acetates;[26] (f) [3+3] benzannulation of 2-(benzotriazol-1-ylmethyl)thiophenes with α, β-unsaturated ketones and aldehydes.[27] Beside these strategies, benzoannelation has been achieved by palladium catalysed cross coupling of 2-stannylthiophenes with chlorocyclobutenone,[28] photochemical addition of thienyl ketene (generated photochemically from α-diazoketone) with an acetylene derivative[29] and cycloaddition of thiophene–carbene chromium complex with alkynes.[30] However, all these methods suffer from limitations like the difficulty in availability of annelation components with suitable substitution pattern, regiochemical control of cycloaddition via thieno *o*-xylene and flexibility of substituent introduction into the benzene ring. Besides, none of these methods can be extrapolated for the general synthesis of more complex polycyclic benzo[*b*]thiophenes.

We have recently reported benzoannelation of 2-methyl-, 3-cyanomethylindole and 2-cyanomethylpyrrole to the corresponding regiospecifically substituted carbazoles[31,32] and indoles[33] utilising α-oxoketene dithioacetals[34] as 3-carbon components in a [3+3] annelation process. These reactions were also found to be efficient for the synthesis of more complex annulated carbazoles and indoles with diverse structural frameworks. Also, we have further shown that depending on the nature of the (indolyl)methyl carbanion the regiochemistry of the reaction (1,4- vs 1,2-addition) can be manipulated leading to either linearly[31] or angularly[32] substituted and annulated carbazoles. Alternatively, the novel oxoketene dithioacetals derived from heterocyclic ketones (i.e. 3-oxoindole[35] or 4-quinolone[36]) could be subjected to benzo-, naphtho- or heteroaromatic annelation with either allyl, benzyl or heteroallyl anions following a similar protocol to efficiently synthesise a variety of polyheterocyclic ring systems. These studies have clearly demonstrated that the oxoketene dithioacetal

Keywords: α-oxoketene dithioacetals; aromatic annelation; benzo[*b*]thiophenes.

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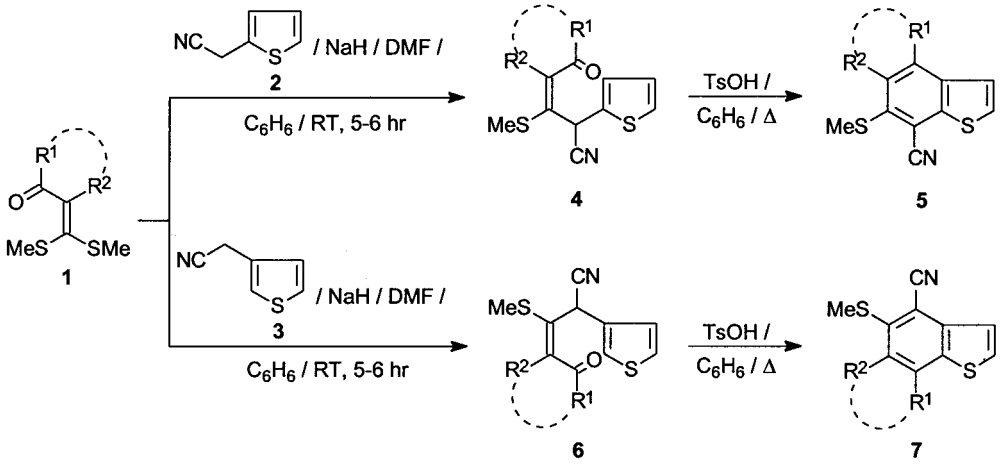

Scheme 1.

Table 1. Synthesis of 4,5,6,7-substituted benzo[*b*]thiophenes

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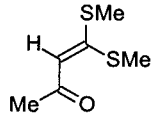
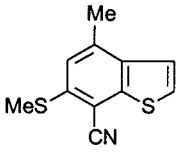
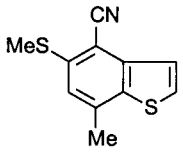
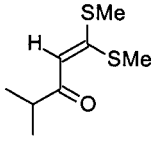
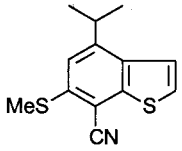
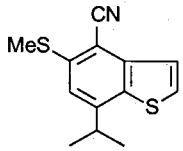
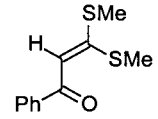
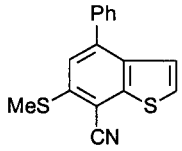
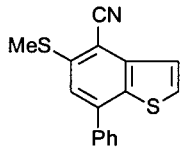
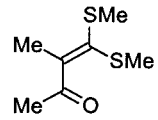
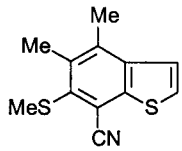
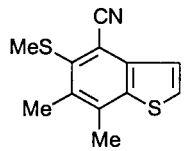
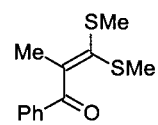
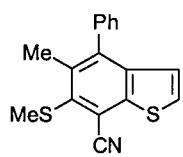
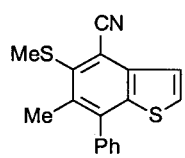
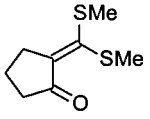
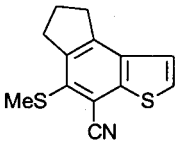
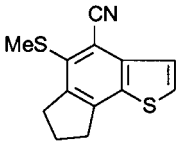
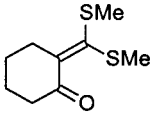
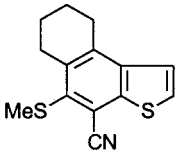
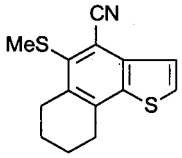
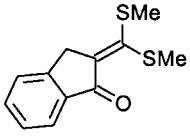
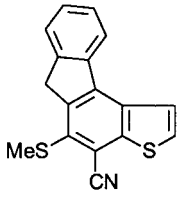
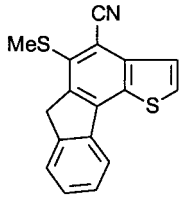
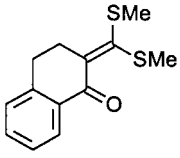
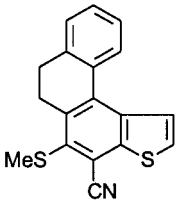
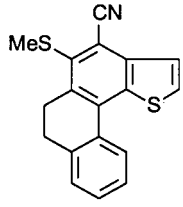
1			
	1a	**5a** (70%)	**7a** (78%)
2			
	1b	**5b** (60%)	**7b** (63%)
3			
	1c	**5c** (72%)	**7c** (87%)
4			
	1d	**5d** (64%)	**7d** (69%)
5			
	1e	**5e** (64%)	**7e** (67%)

Table 2. Synthesis of annelated benzo[*b*]thiophenes

Entry	1	5	7
1			
	1f	**5f** (66%)	**7f** (71%)
2			
	1g	**5g** (60%)	**7g** (65%)
3			
	1h	**5h** (56%)	**7h** (62%)
4			
	1i	**5i** (62%)	**7i** (65%)

mediated aromatic annelation process is a powerful method for the construction of complex heteroaromatics that provides special opportunity for the introduction of substituents into the benzene moiety of heteroaromatics without relying on electrophilic substitution. In continuation of these studies we now wish to report further work designed to extend the utility of our aromatic annelation process for a new highly regiospecific synthesis of polysubstituted and annelated benzo[*b*]thiophenes. The results of these studies are described herein.

Results and Discussion

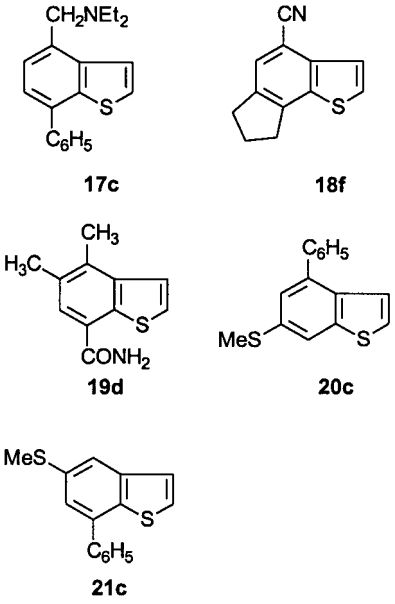
Side chain metallation of methyl substituted thiophene derivatives is normally difficult to achieve because ring metallation is predominant in these reactions. Several substituents are conceivable to stabilise the negative charge in the conjugate base of methylthiophene precursors required for the Michael addition–elimination process with oxoketene dithioacetals. Previous work in our group on the synthesis of carbazoles[32] and indoles[33] has shown that the cyano group is especially useful for this purpose. We therefore selected commercially available 2- and 3-cyanomethylthiophenes as anionic components in the benzoannelation process. Thus in a typical experiment, the oxoketene dithioacetal **1a** was reacted with thiophene-2-acetonitrile **2** in the presence of sodium hydride in DMF/benzene at 0°C to give the adduct **4a** (R^1=Me, R^2=H) in 88% yield. The adduct **4a** underwent smooth cycloaromatization in the presence of *p*-toluenesulfonic acid in refluxing benzene to furnish 7-cyano-4-methyl-6-(methylthio)-benzo[*b*]thiophene **5a** exclusively in 70% yield (Scheme 1, Table 1). The reaction sequence could be extended to the synthesis of other substituted benzo[*b*]thiophenes, i.e. 4-isopropyl- (**5b**), 4-phenyl- (**5c**) and the 4,5,6,7-tetra-substituted derivatives (**5e**) in excellent yields with high regiocontrol of substituent positions. Following a similar protocol, the regioisomeric polysubstituted benzo[*b*]thiophenes **7a–e** could be readily prepared in high yields via benzoannelation of thiophene-3-acetonitrile with appropriate oxoketene dithioacetals (Scheme 1, Table 1). All these benzothiophenes are novel and their structures are fully supported by their NMR spectral and analytical data.

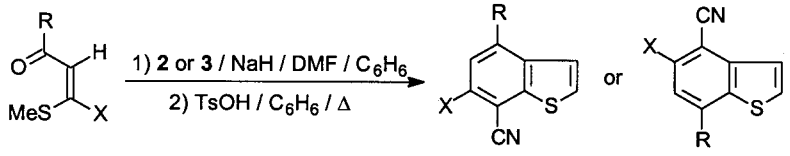
In an extension of this methodology, we next turned our attention to the synthesis of [*e*]- and [*g*]- annelated benzo[*b*]thiophenes by employing oxoketene dithioacetals

1f–i derived from cyclic ketones. Table 2 delineates the versatility of this aromatic annelation strategy for the regiospecific construction of wide range of complex polycyclic benzo[*b*]thiophene systems **5f–i** and **7f–i** in high yields from readily accessible precursors. The methodology provides an easy general entry into these class of compounds which is far superior to the previously reported multistep preparation of the related systems.[23,37]

In a further extension of these studies, benzoannelation of **2** and **3** with a few representative N,S- and O,S-acetals was examined following a similar strategy with a view to extend the scope of this methodology for regiospecific introduction of an amino or alkoxy substituent in the benzene ring of benzo[*b*]thiophene. Thus the 5- and 6-cycloamino and the corresponding 5- and 6-methoxy benzo[*b*]thiophenes were smoothly obtained in high yields from the respective N,S- and O,S-acetals and 2- and 3-cyanomethylthiophenes under the described reaction conditions (Scheme 2, Table 3).

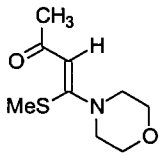
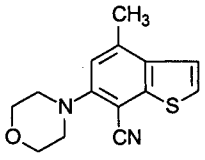
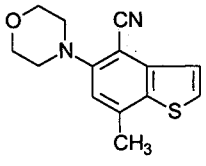
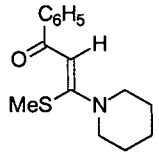
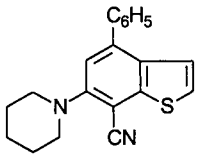
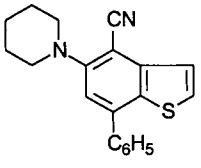
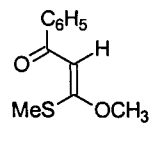
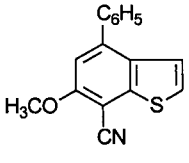
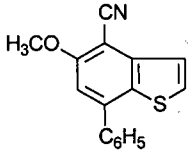
Attempts were made to selectively dethiomethylate the benzo[*b*]thiophenes without affecting the thiophene ring. However, these reactions did not meet with any success and desulfurization with W2 or deactivated Raney Ni or with nickel boride ($NiCl_2$–$NaBH_4$) yielded only inseparable product mixtures in most of the cases except isolation of **17c, 18f** and **19d** on treatment of the corresponding (methylthio)benzothiophenes **7c, 7f** and **5d** with W2 Raney Ni under controlled conditions. As a representative example the nitrile group in **5c** and **7c** could be removed by refluxing them with a mixture of sulfuric and acetic acids in water to provide the corresponding cyanide free benzo[*b*]thiophenes **20c** and **21c** in good yields.





Scheme 2.

Table 3.

Entry	1	5	7
1	 **8a**	 **10a** (67%)	 **11a**(68%)
2	 **9c**	 **12c** (70%)	 **13c** (75%)
3	 **14c**	 **15c** (69%)	 **16c** (71%)

In conclusion, we have demonstrated that the α-oxoketene dithioacetal mediated conjugate addition–cyclization benzoannelation sequence can be used to efficiently synthesise a variety of regioisomeric polysubstituted benzo[*b*]thiophenes from readily available precursors. The methodology could be easily adapted for regiocontrolled synthesis of complex polycyclic benzo[*b*]thiophenes in high yields. Further studies to develop chemoselective catalysts for removal of SMe group in these benzo[*b*]thiophenes are in progress.

Experimental

Melting points were obtained on a Thomas Hoover and Mel-Temp capillary melting point apparatuses and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 983 and Perkin–Elmer-1082 spectrophotometers. NMR spectra were recorded on Bruker ACF-300 and Jeol LA-400 spectrometers. Chemical shifts are reported in δ (ppm) relative to tetramethyl silane and coupling constants (J) are given in Hertz. Mass spectra were obtained on a Jeol D-300 mass spectrometer. Elemental analyses were carried out on a Heraeus CHN–O-Rapid analyzer.

All reactions were monitored by TLC on glass plates coated with silica gel (Acme's) containing 13% calcium sulfate as binder and visualization of compounds was accomplished by exposure to iodine vapour or by spraying potassium permanganate (acidic) solution. Column chromatography was carried out using Acme's silica gel (60–120 mesh).

Thiophene-2-acetonitrile and thiophene-3-acetonitrile were purchased from Aldrich. Oxoketene-S,S-acetals, –N,S-acetals and O,S-acetal were prepared according to the earlier reported procedures.[34]

General procedure for the synthesis of substituted and condensed benzo[*b*]thiophenes

To a stirring suspension of sodium hydride (10 mmol) in DMF (10 mL) and benzene (10 mL) at 0°C, a solution of thiophene-2-acetonitrile or thiophene-3-acetonitrile (5 mmol) in benzene (5 mL) was added dropwise. After 15 min, the appropriate α-oxoketene acetal (5 mmol) in DMF (10 mL) was slowly added and the reaction mixture was allowed to warm to room temperature with stirring during 8–10 h. It was poured into saturated ammonium chloride solution (200 mL) and extracted with benzene (3×50 mL). The combined organic extracts were washed with water (3×100 mL), dried over anhydrous sodium sulfate and evaporated to give the crude 1,4-adducts. The addition–elimination products **4a** and **6a** were purified by passing through silica gel column using hexane–ethyl acetate (19:1) and characterised by spectral and analytical data and the other 1,4-adducts were used as such for further cyclization.

To a solution of crude 1,4-adduct (ca. 5 mmol) in dry benzene (40 mL), *p*-toluenesulfonic acid (10 mmol) was added and the reaction mixture was refluxed with stirring for 3–4 h. The solvent was evaporated, the residue was dissolved in chloroform (100 mL), poured into saturated sodium bicarbonate solution (200 mL). The organic layer was separated, washed with water (2×100 mL), dried over anhydrous sodium sulfate and evaporated to give crude benzo[*b*]thiophene which was purified by column chromatography (silica gel) using hexane–ethyl acetate (97:3) as eluent.

5-Cyano-4-methylthio-5-(2-thienyl)pent-4-en-2-one (4a). Colourless crystals (chloroform–ether); mp 78–79°C; Yield 88%; IR (KBr): 2213, 1710, 1549 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 2.33 (s, 3H), 2.42 (s, 3H), 4.01 (s, 2H), 7.06–7.09 (m, 1H), 7.41–7.46 (m, 2H); ^{13}C NMR (75 MHz): 15.73, 29.46, 49.79, 105.41, 117.47, 126.79, 127.62, 129.67, 135.32, 148.81, 202.08; MS: *m/z* (%): 237 (M^+, 16), 147 (49); Anal. Calcd for $C_{11}H_{11}NOS_2$ (237.35): C, 55.67; H, 4.67; N, 5.90%; Found: C, 55.38; H, 4.70; N, 5.98%.

5-Cyano-4-methylthio-5-(3-thienyl)pent-4-en-2-one (6a). Light yellow liquid; Yield 93%; IR (KBr): 2204, 1705, 1501 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.33 (s, 3H), 2.34 (s, 3H), 3.99 (s, 2H), 7.34–7.43 (m, 2H), 7.63–7.65 (m, 1H); ^{13}C NMR (100 MHz): 15.34, 29.46, 49.67, 105.48, 118.22, 125.66, 126.17, 127.95, 133.01, 151.07, 202.12; MS: *m/z* (%): 237 (M^+, 75); Anal. Calcd for $C_{11}H_{11}NOS_2$ (237.35): C, 55.67; H, 4.67; N, 5.90%; Found: C, 55.94; H, 4.74; N, 5.84%.

7-Cyano-4-methyl-6-(methylthio)benzo[*b*]thiophene (5a). Colourless crystals (chloroform–ether); mp 160–161°C; Yield 70%; IR (KBr): 2207, 1560, 1428 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 2.62 (s, 3H), 2.64 (s, 3H), 7.12 (s, 1H), 7.35 (d, J=5.4 Hz, 1H), 7.47 (d, J=5.4 Hz, 1H); ^{13}C NMR (75 MHz): 17.00, 20.24, 116.03, 122.27, 124.16, 126.71, 126.77, 137.54, 138.29, 140.63, 143.72; MS: *m/z* (%): 219 (M^+, 100); Anal. Calcd for $C_{11}H_9NS_2$ (219.33): C, 60.24; H, 4.14; N, 6.39%; Found: C, 60.43; H, 4.19; N, 6.23%.

4-Cyano-7-methyl-5-(methylthio)benzo[*b*]thiophene (7a). Colourless crystals (chloroform–ether); mp 150–151°C; Yield 78%; IR (KBr): 2208, 1649, 1562, 1421 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 2.62 (s, 6H), 7.15 (s, 1H), 7.53 (d, J=6.0 Hz, 1H), 7.65 (d, 1H, J=6.0 Hz); MS: (*m/z*, %): 219 (M^+, 100); Anal. Calcd for $C_{11}H_9NS_2$ (219.33): C, 60.24; H, 4.14; N, 6.39%; Found: C, 60.49; H, 4.18; N, 6.43%.

7-Cyano-6-methylthio-4-*i*-propylbenzo[*b*]thiophene (5b). Colourless crystals (chloroform–ether); mp 106–107°C; Yield 60%; IR (KBr): 2207, 1564, 1428 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 1.39 (d, J=7.1 Hz, 6H), 2.65 (s, 3H), 3.48 (septet, J=7.1 Hz, 1H), 7.26 (s, 1H), 7.46 (d, J=5.6 Hz, 1H), 7.51 (d, J=5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 17.35, 22.95, 31.91, 104.01, 116.05, 120.46, 121.97, 126.81, 136.66, 140.69, 144.14, 148.80; MS: *m/z* (%): 247 (M^+, 100); Anal. Calcd for $C_{13}H_{13}NS_2$ (247.38): C, 63.12; H, 5.30; N, 5.66%; Found: C, 63.39; H, 5.23; N, 5.77%.

4-Cyano-5-(methylthio)-7-*i*-propylbenzo[*b*]thiophene (7b). Yellow crystals (chloroform–ether); mp 56–57°C; Yield 63%; IR (KBr): 2215, 1546, 1429 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 1.42 (d, J=6.6 Hz, 6H), 2.64 (s, 3H),

3.25 (brm, 1H), 7.24 (s, 1H), 7.48 (brm, 1H), 7.62 (brm, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 17.23, 22.29, 33.96, 104.36, 116.49, 119.78, 122.64, 130.02, 136.84, 140.93, 141.68, 148.01; MS: (*m/z*, %): 247 (M^+, 100); Anal. Calcd for $C_{13}H_{13}NS_2$ (247.38): C, 63.12; H, 5.30; N, 5.66%; Found: C, 63.34; H, 5.34; N, 5.74%.

7-Cyano-6-(methylthio)-4-phenylbenzo[*b*]thiophene (5c). Colourless crystals (chloroform–ether); mp 141–142°C; Yield 72%; IR (KBr): 2213, 1550, 1422 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 2.63 (s, 3H), 7.28 (s, 1H), 7.36 (d, *J*=5.5 Hz, 1H), 7.42–7.52 (m, 6H); ^{13}C NMR (75 MHz): 16.83, 104.20, 115.84, 123.54, 123.61, 127.00, 128.65, 128.81, 136.09, 138.98, 140.80, 141.90, 144.60; MS: *m/z* (%): 281 (M^+, 100); Anal. Calcd for $C_{16}H_{11}NS_2$ (281.40): C, 68.29; H, 3.94; N, 4.98%; Found: C, 68.60; H, 3.87; N, 5.03%.

4-Cyano-5-(methylthio)-7-phenylbenzo[*b*]thiophene (7c). Colourless crystals; mp 111–112°C; Yield 87%; IR (KBr): 2208, 1558, 1418 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 2.66 (s, 3H), 7.34 (s, 1H), 7.49–7.60 (m, 4H), 7.67–7.71 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 17.10, 109.30, 116.40, 122.70, 123.10, 128.10, 129.10, 129.30, 131.50, 136.80, 138.80, 141.20, 142.30; MS: (*m/z*, %): 281 (M^+, 100); Anal. Calcd for $C_{16}H_{11}NS_2$ (281.40): C, 68.29; H, 3.94; N, 4.98%; Found: C, 68.55; H, 3.98; N, 5.04%.

7-Cyano-4,5-dimethyl-6-(methylthio)benzo[*b*]thiophene (5d). Colourless crystals (chloroform–ether); mp 115–116°C; Yield 64%; IR (KBr): 2209, 1547, 1416 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 2.43 (s, 3H), 2.58 (s, 3H), 2.60 (s, 3H), 7.37 (d, *J*=5.5 Hz, 1H), 7.51 (d, *J*=5.5 Hz, 1H); ^{13}C NMR (75 MHz): 17.55, 18.11, 19.96, 110.41, 116.95, 122.77, 127.98, 136.42, 137.03, 139.97, 140.81; MS: (*m/z*, %): 233 (M^+, 100); Anal. Calcd for $C_{12}H_{11}NS_2$ (233.36): C, 61.76; H, 4.75; N, 6.00%; Found: C, 61.48; H, 4.78; N, 6.06%.

4-Cyano-6,7-dimethyl-5-(methylthio)benzo[*b*]thiophene (7d). Colourless crystals (chloroform–ether); mp 123–125°C; Yield 64%; IR (KBr): 2205, 1470, 1440 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 2.46 (s, 3H), 2.59 (s, 3H), 2.60 (s, 3H), 7.51 (d, 1H, *J*=5.6 Hz), 7.55 (d, 1H, *J*=5.5 Hz); ^{13}C NMR (100 MHz): 17.56, 19.78, 19.95, 111.19, 117.41, 123.35, 128.94, 135.84, 135.99, 137.63, 139.33, 141.72; MS: (*m/z*, %): 233 (M^+, 100); Anal. Calcd for $C_{12}H_{11}NS_2$ (233.36): C, 61.76; H, 4.75; N, 6.00%; Found: C, 61.54; H, 4.78; N, 5.95%.

7-Cyano-5-methyl-6-(methylthio)-4-phenylbenzo[*b*]thiophene (5e). Colourless crystals (chloroform–ether); mp 124–125°C; Yield 64%; IR (KBr): 2921, 2214, 1485, 1440 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 2.45 (s, 3H), 2.55 (s, 3H), 6.88 (d, *J*=5.4 Hz, 1H), 7.25–7.28 (m, 2H), 7.43–7.53 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 18.84, 19.80, 112.04, 116.75, 124.35, 127.97, 128.05, 128.60, 128.88, 136.09, 137.86, 138.88, 140.09, 141.06, 141.68; MS: *m/z* (%): 295 (M^+, 78), 233 (100); Anal. Calcd for $C_{17}H_{13}NS_2$ (295.43): C, 69.12; H, 4.44; N, 4.74%; Found: C, 69.41; H, 4.36; N, 4.82%.

4-Cyano-6-methyl-5-(methylthio)-7-phenylbenzo[*b*]thiophene (7e). Colourless crystals (chloroform–hexane); mp 122–123°C; Yield 67%; IR (KBr): 2209, 1535, 1447 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 2.47 (s, 3H), 2.54 (s, 3H), 7.32 (d, 1H, *J* = 1.6 Hz), 7.47–7.52 (m, 3H), 7.54–7.55 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 18.82, 19.71, 112.32, 117.12, 122.69, 128.42, 128.91, 130.42, 135.38, 138.21, 139.50, 140.80, 142.24; MS: (*m/z*, %): 295 (M^+, 100); Anal. Calcd for $C_{17}H_{13}NS_2$ (295.43): C, 69.12; H, 4.44; N, 4.74%; Found: C, 69.35; H, 4.38; N, 4.70%.

4-Cyano-7,8-dihydro-5-methylthio-6*H*-indeno[5,4-*b*]thiophene (5f). Colourless crystals (chloroform–ether); mp 129–130°C; Yield 66%; IR (KBr): 2213, 1549, 1428 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 2.44 (quintet, *J*=7.5 Hz, 2H), 2.54 (s, 3H), 3.15 (t, *J*=7.5 Hz, 2H), 3.24 (t, *J*=7.6 Hz, 2H), 7.25 (d, *J*=5.6 Hz, 1H), 7.53 (d, *J*=5.6 Hz, 1H); ^{13}C NMR (75 MHz): 19.06, 24,39, 33.07, 33.20, 108.62, 116.90, 122.10, 128.57, 134.26, 136.29, 142.78, 143.67, 144.23; MS: *m/z* (%): 245 (M^+, 100); Anal. Calcd for $C_{13}H_{11}NS_2$ (245.37): C, 63.64; H, 4.52; N, 5.71%; Found: C, 63.86; H, 4.59; N, 5.67%.

4-Cyano-7,8-dihydro-5-methylthio-6*H*-indeno[4,5-*b*]thiophene (7f). Colourless crystals (chloroform–ether); mp °C; Yield 71%; IR (KBr): 2208, 1562, 1421 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): 2.25 (pentet, *J*=7.6 Hz, 2H), 2.52 (s, 3H), 3.10–3.18 (m, 4H), 7.45 (d, *J*=5.6 Hz, 1H), 7.54 (d, *J*=5.6 Hz, 1H); ^{13}C NMR (100 MHz): 18.81, 24.06, 33.21, 33.27, 109.12, 117.11, 122.57, 129.04, 134.04, 135.73, 141.15, 142.35, 143.63; MS: *m/z* (%): 245 (M^+, 100); Anal. Calcd for $C_{13}H_{11}NS_2$ (245.37): C, 63.64; H, 4.52; N, 5.71%; Found: C, 63.87; H, 4.57; N, 5.78%.

4-Cyano-5-(methylthio)-6,7,8,9-tetrahydronaphtho[2,1-*b*]thiophene (5g). Colourless crystals(chloroform–ether); mp 136–137°C; Yield 60%; IR (KBr): 2925, 2213, 1535, 1428 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 1.88–1.90 (brm, 4H), 2.47 (s, 3H), 3.03–3.07 (brm, 4H), 7.34 (d, *J*=5.5 Hz, 1H), 7.52 (d, *J*=5.5 Hz, 1H); ^{13}C NMR (75 MHz): 19.63, 22.06, 22.88, 28.07, 28.31, 110.12, 116.90, 121.88, 128.19, 136.83, 137.60, 137.67, 139.40, 140.39; MS: *m/z* (%): 259 (M^+, 100); Anal. Calcd for $C_{14}H_{13}NS_2$ (259.40): C, 64.83; H, 5.05; N, 5.40%; Found: C, 65.09; H, 5.02; N, 5.35%.

4-Cyano-5-(methylthio)-6,7,8,9-tetrahydronaphtho[1,2-*b*]thiophene (7g). Colourless crystals (chloroform–ether); mp 131–132°C; Yield 65%; IR (KBr): 2205, 1525, 1440 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 1.91–1.93 (m, 4H), 2.48 (s, 3H), 2.93–2.95 (m, 2H), 3.07–3.08 (m, 2H), 7.50 (d, 1H, *J*=5.6 Hz), 7.53 (d, 1H, *J*=5.5 Hz); ^{13}C NMR (100 MHz): 19.59, 22.04, 23.19, 28.32, 29.07, 110.87, 117.29, 123.03, 128.59, 136.43, 136.73, 137.79, 139.04, 140.77; MS: (*m/z*, %): 259 (M^+, 82), 233 (100); Anal. Calcd for $C_{14}H_{13}NS_2$ (259.40): C, 64.83; H, 5.05; N, 5.40%; Found: C, 65.06; H, 5.11; N, 5.46%.

4-Cyano-5-(methylthio)fluoreno[3,4-*b*]thiophene (5h). Colourless crystals (chloroform–ether); mp 210–211°C; Yield 56%; IR (KBr): 2212, 1531, 1479 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 2.65 (s, 3H), 4.04 (s, 2H), 7.42–7.52 (m, 2H), 7.65 (d, *J*=7.3 Hz, 1H), 7.73 (d, *J*=5.5 Hz, 1H), 7.94 (d, *J*=5.5 Hz, 1H), 8.06 (d, *J*=7.2 Hz, 1H); ^{13}C NMR (75 MHz): 19.26, 37.71, 108.48, 116.92, 121.46, 122.85, 125.19, 127.37, 128.28, 129.36, 133.46, 134.16, 139.49,

140.41, 143.46, 144.38, 144.62; MS: *m/z* (%): 293 (M^+, 79), 246 (100); Anal. Calcd for $C_{17}H_{11}NS_2$ (293.41): C, 69.59; H, 3.78; N, 4.77%; Found: C, 69.34; H, 3.70; N, 4.85%.

4-Cyano-5-(methylthio)fluoreno[4,3-*b*]thiophene (7h). Colourless crystals (chloroform–ether); mp 214–215°C; Yield 62%; IR (KBr): 2210, 1567, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.59 (s, 3H), 3.92 (s, 2H), 7.38–7.46 (m, 2H), 7.54 (d, 2H, *J*=4.5 Hz), 7.63 (d, 1H, *J*=5.2 Hz), 7.79 (d, 1H, *J*=6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 19.07, 37.90, 109.01, 117.31, 122.47, 124.90, 127.28, 128.32, 131.84, 134.17, 138.99, 139.20, 142.52, 142.60, 144.06; MS: (*m/z*, %): 293 (M^+, 88.9); Anal. Calcd for $C_{17}H_{11}NS_2$ (293.41): C, 69.59; H, 3.78; N, 4.77%; Found: C, 69.83; H, 3.73; N, 4.71%.

4-Cyano-6,7-dihydro-5-(methylthio)phenanthro[3,4-*b*]thiophene (5i). Colourless crystals (chloroform–ether); mp 132–133°C; Yield 62%; IR (KBr): 2207, 1549, 1427 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 2.46 (s, 3H), 2.77–2.82 (m, 2H), 3.17–3.22 (m, 2H), 7.34–7.37 (m, 3H), 7.60 (d, *J*=5.6 Hz, 1H), 7.83 (d, *J*=5.6 Hz, 1H), 7.83–7.85 (m, 1H); ^{13}C NMR (75 MHz): 19.80, 27.15, 28.90, 111.2, 116.87, 124.14, 126.72, 127.82, 128.79, 128.92, 133.46, 135.58, 136.04, 136.44, 139.03, 139.57, 143.28; MS: *m/z* (%): 307 (M^+, 100); Anal. Calcd for $C_{18}H_{13}NS_2$ (307.44): C, 70.32; H, 4.26; N, 4.56%; Found: C, 70.53; H, 4.29; N, 4.49%.

4-Cyano-6,7-dihydro-5-(methylthio)phenanthro[4,3-*b*]-thiophene (7i). Colourless crystals (chloroform–ether); mp 122–123°C; Yield 65%; IR (KBr): 2210, 1567, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.48 (s, 3H), 2.84 (t, 2H, *J*=6.8 Hz), 3.30 (t, 2H, *J*=6.8 Hz), 7.25–7.45 (m, 3H), 7.61–7.66 (m, 3H), 8.27 (d, 1H, *J*=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 19.85, 27.15, 28.68, 112.00, 117.36, 123.03, 126.16, 126.90, 128.06, 129.77, 133.13, 134.83, 136.66, 136.95, 138.26, 139.59, 141.52; MS: (*m/z*, %): 307 (M^+, 81), 259 (100); Anal. Calcd for $C_{18}H_{13}NS_2$ (307.44): C, 70.32; H, 4.26; N, 4.56%; Found: C, 70.57; H, 4.21; N, 4.48%.

7-Cyano-4-methyl-6-(4-morpholino)benzo[*b*]thiophene (10a). Colourless crystals (chloroform–ether); mp 141–143°C; Yield 67%; IR (KBr): 2205, 1572, 1440 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 2.62 (s, 3H), 3.25–3.28 (m, 4H), 3.89–3.93 (m, 4H), 6.85 (s, 1H), 7.30 (d, *J*=5.5 Hz, 1H), 7.36 (d, *J*=5.5 Hz, 1H); ^{13}C NMR (75 MHz): 20.42, 52.22, 66.96, 96.21, 116.40, 117.19, 122.07, 125.02, 134.47, 139.10, 144.31, 154.08; MS: *m/z* (%): 258 (M^+, 71), 200 (100); Anal. Calcd for $C_{14}H_{14}N_2OS$ (258.34): C, 65.09; H, 5.46; N, 10.84%; Found: C, 65.37; H, 5.42; N, 10.77%.

4-Cyano-7-methyl-5-(4-morpholino)benzo[*b*]thiophene (11a). Colourless crystals (chloroform–ether); mp 91–92°C; Yield 68%; IR (KBr): 2201, 1579 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.63 (s, 3H), 3.27 (t, 4H, *J*=4.4 Hz), 3.91 (t, 4H, *J*=4.4 Hz), 6.84 (s, 1H), 7.30 (d, 1H, *J*=5.2 Hz), 7.36 (d, 1H, *J*=5.2 Hz); ^{13}C NMR (100 MHz): 20.39, 52.27, 66.94, 96.56, 116.36, 116.96, 121.95, 125.09, 134.51, 138.86, 144.49, 154.06; MS: (*m/z*, %): 258 (M^+, 100); Anal. Calcd for $C_{14}H_{14}N_2OS$ (258.34): C, 65.09; H, 5.46; N, 10.84%; Found: C, 65.31; H, 5.52; N, 10.95%.

7-Cyano-4-phenyl-6-(1-piperidino)benzo[*b*]thiophene (12c). Colourless crystals (chloroform–ether); mp 151–152°C; Yield 70%; IR (KBr): 2212, 1565, 1448 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 1.61–1.67 (m, 2H), 1.76–1.81 (m, 4H), 3.28–3.32 (m, 4H), 7.00 (s, 1H), 7.30 (s, 2H), 7.43–7.54 (m, 5H); ^{13}C NMR (75 MHz): 24.06, 26.19, 53.53, 97.03, 116.66, 117.40, 123.37, 124.68, 138.33, 128.68, 128.78, 132.30, 139.80, 142.36, 145.41, 155.34; MS: *m/z* (%): 318 (M^+, 100); Anal. Calcd for $C_{20}H_{18}N_2S$ (318.44): C, 75.44; H, 5.70; N, 8.80%; Found: C, 75.76; H, 5.77; N, 8.73%.

4-Cyano-7-phenyl-5-(1-piperidino)benzo[*b*]thiophene (13c). Colourless crystals (chloroform–ether); mp 141–142°C; Yield 75%; IR (KBr): 2212, 1565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 1.62–1.63 (m, 2H), 1.80–1.81 (m, 4H), 3.30–3.32 (m, 4H), 7.00 (s, 1H), 7.29 (s, 2H), 7.44–7.51 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): 24.03, 26.15, 53.47, 96.99, 116.62, 117.33, 123.33, 124.63, 128.27, 128.62, 128.72, 132.27, 139.78, 142.32, 145.38, 155.27; MS: (*m/z*, %): 318 (M^+, 100); Anal. Calcd for $C_{20}H_{18}N_2S$ (318.44): C, 75.44; H, 5.70; N, 8.80%. Found: C, 75.71; H, 5.66; N, 8.72%.

7-Cyano-6-methoxy-4-phenylbenzo[*b*]thiophene (15c). Colourless crystals (chloroform–ether); mp 115–116°C; Yield 69%; IR (KBr): 2214, 1597, 1413 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 4.04 (s, 3H), 7.02 (s, 1H), 7.33 (d, 1H, *J*=5.2 Hz), 7.37 (d, 1H, *J*=5.4 Hz) 7.49–7.54 (m, 5H); MS: (*m/z*, %): 265 (M^+, 100), 222 (42.7); Anal. Calcd for $C_{16}H_{11}NOS$ (265.34): C, 72.43; H, 4.18; N, 5.28%; Found: C, 72.66; H, 4.25; N, 5.44%.

4-Cyano-5-methoxy-7-phenylbenzo[*b*]thiophene (16c). Colourless crystals (chloroform–ether); mp 119–120°C; Yield 71%; IR (KBr): 2204, 1575, 1430 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 4.05 (s, 3H), 7.04 (s, 1H), 7.48–7.56 (m, 4H), 7.69–7.72 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 56.84, 109.78, 115.32, 123.37, 125.31, 125.34, 128.66, 128.83,132.56, 139.57, 143.35, 144.77; MS: (*m/z*, %): 265 (M^+, 100); Anal. Calcd for $C_{16}H_{11}NOS$ (265.34): C, 72.43; H, 4.18; N, 5.28%; Found: C, 72.12; H, 4.55; N, 5.34%.

4-(Diethylamino)methyl-7-phenylbenzo[*b*]thiophene (17c). To a solution of **7c** (2.5 mmol) in absolute ethanol (30 mL), Raney Ni (W2, six times by weight) was added and the suspension was refluxed for 5 h (monitored by TLC). The reaction mixture was filtered through sintered funnel and the residue was washed with ethanol. The bulk of the ethanol was distilled off and chloroform was added. The solution was washed with water, dried over anhydrous sodium sulphate, concentrated and the crude product obtained was passed through silica gel column using hexane–ethyl acetate (19:1) as eluent. Yellow crystals (chloroform–ether); mp 71–72°C; Yield 68%; IR (KBr): 2900, 1650, 1600, 1550 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 1.07 (t, 6H), 2.61 (q, 4H), 3.92 (s, 2H), 7.31–7.50 (m, 6H), 7.71 (m, 3H); MS: (*m/z*, %): 295 (M^+, 52), 223 (100); Anal. Calcd for $C_{19}H_{21}NS$ (295.44): C, 77.24; H, 7.16; N, 4.74%; Found: C, 77.40; H, 7.29, N, 4.56%.

4-Cyano-7,8-dihydro-6*H*-indeno[4,5-*b*]thiophene (18f). Colourless crystals (chloroform–ether); mp 101–102°C;

Yield 55%; IR (KBr): 2200, 1579 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.26–2.31 (m, 2H), 3.08 (m, 4H), 7.55–7.75 (m, 3H); MS: (*m/z*, %): 199 (M^+, 100); Anal. Calcd for $C_{12}H_9NS$ (199.27): C, 72.33; H, 4.55; N, 7.02%; Found: C, 72.55; H, 4.67; N, 7.11%.

4,5-Dimethylbenzo[*b*]thiophene-7-carboxamide (19d). Procedure is same as that of **17c** except that rectified spirit is used instead of absolute ethanol. Colourless solid (chloroform–hexane); mp 220–221°C; Yield 66%; IR (KBr): 3412, 3195, 2922, 1641, 1610, 1412 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.46 (s, 3H), 2.59 (s, 3H), 6.00 brs, 2H), 7.45 (d, *J*=5.6 Hz, 1H), 7.48 (s, 1H), 7.57 (d, *J*=5.6 Hz, 1H); MS: *m/z* (%): 205 (M^+, 100); Anal Calcd for $C_{11}H_{11}NOS$ (205.28): C, 64.36; H, 5.40; N, 6.82%; Found: C, 64. 62; H, 5.35; N, 6.90%.

Procedure for decyanation of 5c and 7c

To a mixture of sulfuric acid (5 mL), acetic acid (5 mL) and water (5 mL), compound **5c** or **7c** (2.5 mmol) was added and the mixture was heated at 180°C for 8 h. It was then diluted with water, extracted with chloroform, washed with water, dried and evaporated. The residue obtained was passed through silica gel column using hexane as eluent.

6-Methylthio-4-phenylbenzo[*b*]thiophene (20c). Colourless viscous liquid; IR (CH_2Cl_2): 1610, 1575, 1430 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.50 (s, 3H), 7.24–7.27 (m, 2H), 7.30–7.37 (m, 2H), 7.39–7.45 (m, 2H), 7.49–7.52 (m, 2H), 7.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 16.50, 119.01, 123.01, 124.39, 125.33, 127.54, 128.46, 128.90, 134.68, 135.72, 137.84, 140.34, 141.35; MS: (*m/z*, %): 256 (M^+, 100); Anal Calcd for $C_{15}H_{12}S_2$ (256.39): C, 70.27; H, 4.72%; Found: C, 70.51; H, 4.65%.

5-Methylthio-7-phenylbenzo[*b*]thiophene (21c). Colourless viscous liquid; IR (CH_2Cl_2): 1585, 1443 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 2.52 (s, 3H), 7.24–7.27 (m, 2H), 7.30–7.37 (m, 2H), 7.39–7.45 (m, 2H), 7.49–7.52 (m, 2H), 7.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 16.50, 119.01, 123.01, 124.39, 125.33, 127.54, 128.46, 128.90, 134.68, 135.72, 137.84, 140.34, 141.35; MS: (*m/z*, %): 256 (M^+, 100); Anal Calcd for $C_{15}H_{12}S_2$ (256.39): C, 70.27; H, 4.72%; Found: C, 70.01; H, 4.84%.

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