CHAPTER IV

"A NEW EFFICIENT SYNTHESIS OF SUBSTITUTED AND CONDENSED BENZO[h]THIOPHENES"
Benzo[b]thiophene 1 and some of its derivatives have been first discovered in coal tar and in various petroleum crude oils. Its first synthesis was reported by Gatterman and Lockhart in 1893 by involving diazotization of α-amino-ω-chlorostyrene 2 to the corresponding thiophenol 3 which underwent intramolecular base catalyzed cyclization to yield benzo[b]thiophene 1 (scheme 1).

Several benzo[b]thiophenes have been recognized as biologically active agents as bioisosters of indoles. Thus a number of benzo[b]thiophene analogues of biologically active indole derivatives have proved to be agonists or antagonists of indole derivatives.

![Scheme 1](image)

In the last 100 years, many synthetic methods have been developed for the synthesis of benzo[b]thiophenes. They can be classified as two major groups as follows.

1) Starting from benzene and its derivatives and build thiophene ring to afford the benzo[b]thiophenes.
2) Starting from preconstructed thiophene and its derivatives and build the aromatic ring to afford the corresponding benzo[b]thiophenes.

The first method suffers from serious limitations which requires functionalization of benzene ring at two carbon atoms ortho to each other and this process is particularly difficult when the product benzo[b]thiophene contains substituent/substituents due to problems associated in aromatic orientation. On the other hand, the second approach for the synthesis of benzo[b]thiophene based on preconstructed thiophene ring over which appropriately substituted benzene ring could be created. This method is of particular interest because one can manipulate the substituents in newly formed benzene ring by appropriately placing them in open chain precursors. Besides, this approach has further support since the required thiophene is easily available in large quantities from coal products. The advantage of the methodology for the synthesis of benzo[b]thiophenes starting from functionalized thiophene derivatives can provide greater regiocontrolled of substituents in the newly formed benzene ring as illustrated in the following four schemes. In scheme 2, the benzo[b]thiophene 7 is a possible product when α-oxoketene dithioacetal 5 reacts with thiophene-3-acetonitrile 4 while the corresponding thiophene-2-acetonitrile 4A when reacted with 5 will yield another regioisomer 7a exclusively. These possibilities allow us to achieve the synthesis of benzo[b]thiophene with full controlled on the substituents. The scheme 2 and 3 illustrates only part of the regiocontrol. The other two
possibilities are described in scheme 4 and 5 where the 2-lithiomethylthiophene will react with 5 in the 1,2-fashion to afford the corresponding carbinol acetal 6 which on acid assisted cyclization should yield benzo[b]thiophene with $R^1$ at 5 and $R^2$ at 6 positions. If one consider all the
four possibilities of substituents in scheme 2-5, it is clear in scheme 2, R\(^1\) and R\(^2\) are at 7 and 6 positions respectively and they can be moved on 4 and 5 position in 7A and 6 and 5 position in 7B and 5 and 6 position in 7c is a remarkable regiocontrolled of our methodology heteroaromatic annulation particularly making benzene ring over preconstructed thiophene derivatives. We have already investigated the reaction of thiophene-2-acetonitrile with 5 and confirmed the formation of expected regioisomer 7A (scheme 3) in unequivocal terms. We have investigated in the present investigation, the

![Scheme 4](image)

reaction of thiophene-3-acetonitrile with 5 so that regiocontrol can now moved at 7 and 6 positions from 4 and 5 positions in the newly formed benzene rings.

We therefore briefly discuss various literature methods based on construction of benzo[b]thiophenes from the preconstructed thiophene derivatives.
Fieser and co-workers\textsuperscript{11} reported in 1935 the synthesis of 4-hydroxybenzo[b]thiophene 12 as illustrated in scheme 6. Thus on subjecting thiophene 8 with succinic anhydride under Friedel Craft's reaction conditions to afford good yield of β-(α-thienoyl)propionic acid 9 which on Clemmenson
reduction afforded $\gamma$-($\alpha$-thienyl)butyric acid $10$. The acid $10$ was then treated with thionyl chloride and stannic chloride yielded the corresponding 4-oxo-4,5,6,7-tetrahydrobenzo[$b$]thiophene $11$ in good yield (scheme 6). The tetrahydro compound $11$ on sulphur dehydrogenation yielded the corresponding 4-hydroxybenzo[$b$]thiophene $12$. Similarly Mc Dowell and co-workers$^{12}$ have developed a method for the synthesis of 7-oxo-tetrahydrobenzo[$b$]thiophene starting from 3-acetylthiophene.

2-Vinyl thiophene $13$ (scheme 7) has been used by Scully and Brown$^{13}$ for benzothiophene synthesis by Diels-Alder cycloaddition approach. Thus maleic anhydride and 2-vinylthiophene $13$ were refluxed in benzene to afford the corresponding cycloadduct $14$ along with some polymeric material. The anhydride was then hydrolyzed to the corresponding tetrahydro dicarboxylic acid $15$ which on S dehydrogenation yielding the corresponding anhydride of benzo[$b$]thiophene $16$. The anhydride on further hydrolysis and
decarboxylation yielded the desired benzo[b]thiophene 1 in over all moderate yield. Seitz and co-workers\textsuperscript{14} also reacted 2-vinylthiophene 14 with tetrabromocyclopropene to afford the cycloadducts which undergoes cyclopropane ring cleavage selectively at C-1/C-3 to afford functionalized benzothiophene.

There are several methods for the synthesis of benzo[b]thiophene systems based on the quinodimethane approach using various functionalized thiophenes 17,\textsuperscript{15-16} 18,\textsuperscript{17-19} 19,\textsuperscript{20} 20\textsuperscript{21} etc. (scheme 8). All these dienes and their precursors were reacted with various dienophiles to afford the corresponding
dihydro or tetrahydro benzo[b]thiophenes which were subsequently transformed into the corresponding benzo[b]thiophenes 21, 22, 23 and 24 as illustrated in scheme 8.

An intramolecular Diels-Alder reaction was designed for the synthesis of annelated benzo[b]thiophene 30. Thus 2,3-dibromothiophene 25 was reacted with DMF in the presence of n-BuLi to afford the corresponding 2-aldehyde amino acetal 26. It was then reacted with heptenal to get the

Corresponding tetrahydronaphtho[2,1-b]thiophene 30 involving formation of furano thiophene 28 and its cycloadduct 29 followed by elimination of water.

Similarly intramolecular Diels-Alder approach was used for the synthesis of 6,7-cyclopentano-4-(ethylthio)benzo[b]thiophene 36 in the recent year (1996). Thus 3-methylthiophene-2-carboxylic acid 31 was converted
into its amide 32 followed by bromination using N-bromo succinimide and reaction with ethanol to afford 33. 5-Pentylmagnesium bromide was then reacted with amide 33 to get the corresponding ketone 34. The ketone was then treated with acetic anhydride and PTSA to yield the benzo[b]thiophene 36 involving the formation of furan ring cycloaddition and dehydration in one step.

Lebieskind and co-workers\textsuperscript{30} have described an interesting benzoannulation approach for the synthesis of functionalized
benzo[b]thiophene. Thus 4-chloro-2,3-diethyl-2-cyclobutanone 37 underwent palladium catalyzed cross coupling with 5-trimethylsilyl-2-tributylstannylthiophene 38. The intermediate on thermolysis yielded the corresponding benzo[b]thiophene in 58% yield.

Katritzky and co-workers\textsuperscript{31} have used 2-(benzotriazol-1-ylmethyl)thiophenes 88 for the synthesis of benzo[b]thiophenes as formulated in scheme 12. These functionalized thiophenes were easily obtained by condensation of 1-(hydroxymethyl)benzotriazole with thiophenes. Lithiation of these intermediates 88 followed by reaction of the resulting anions to various unsaturated aldehydes and ketones yielded the corresponding 1,4-adducts 89 which on subsequent acid catalyzed intramolecular cyclization
followed by debenzotriazolization-dehydration afforded polysubstituted benzo[b]thiophenes 90 in high yields.

Recently we developed a facile general method for the synthesis of benzo[b]thiophenes based on heteroaromatic annulation protocol. There are several possibilities as described in scheme 3 and 4 to generate various allyl anions which can be reacted with α-oxoketene dithioacetals following one of the two possibilities. We have described from our laboratory one such possibilities involving the reaction of thiophene-2-acetonitrile 4A with α-oxoketene dithioacetals in the presence of NaH and DMF at ambident temperatures to afford the corresponding addition elimination products 6A in excellent yields. These intermediates were then cyclized by refluxing in the presence of TsOH in benzene to afford the corresponding regioselectively substituted 7-cyanobenzo[b]thiophenes 7A in high yields (scheme 13).
PRESENT WORK

We have described in the preceding section, some of the important methods for the synthesis of benzo[b]thiophenes based on thiophene or its derivatives as starting materials. Among all, the methods based on cycloaddition reactions have been extensively studied using vinylthiophenes or orthoquinodimethane intermediates as dienes to afford, generally, tetrahydrobenzo[b]thiophenes. Therefore, an additional step of dehydrogenation was inevitably used affecting adversely the overall yields of the desired products. Though the cycloadducts were obtained in high yields, the preparation of the quinodimethane precursors generally involved complex multistep organic reactions reducing the yields of final products. Thus all the
methods do not enjoy preparatory status due to the overall low yields. Also in some cases, particularly the cycloaddition of vinyl thiophenes is reported to yield the regioisomers creating problem of their separation. On the other hand the heteroaromatic annulation methodology developed in our laboratory stands superior to those described in the literature. Particularly in its simplicity less number of steps and high yields of benzo[b]thiophenes retaining the regiocontrol of the substituents at 4, 5, 6 and 7 positions. In the present investigation, we considered of interest to examine the reaction of thiophene-3-acetonitrile with various \( \alpha \)-oxoketene dithioacetals in order to accomplish the alternative possible regioisomers of benzo[b]thiophenes. These new benzo[b]thiophenes will carry substituents at 7 and 6 positions along with cyano and methylthio groups at 4 and 5 positions respectively. These reactions have been investigated in the present work and described below.

In a typical experiment thiophene-3-acetonitrile 4 (scheme 14) was reacted with acetophenone mercaptal 5a in the presence of \( \text{NaH} \) in DMF at ice cool temperature for 8 h. The reaction mixture after work up yielded the corresponding addition elimination product 6a in 89 % yield. The structure of 6a was fully confirmed by its spectral and analytical data to establish the generality of the formation of these intermediates with other \( \alpha \)-oxoketene dithioacetals and they were not characterized in subsequent reactions. The analytical and spectral data for 6a are described below.
Colourless crystals; m.p. 78-79 °C (chloroform-ether)

IR (KBr): $\nu_{\text{max}}$ 2213, 1710, 1549 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.42 (s, 3H), 4.01 (s, 2H), 7.06-7.09 (m, 1H), 7.41-7.46 (m, 7H).

Anal. Calcd. for C$_{16}$H$_{13}$NOS$_2$ (299.35): C, 55.67; H, 4.67; N, 5.90%. Found: C, 55.28; H, 4.70; N, 5.94%.

The addition elimination product 6a was then subjected to cycloaromatization by refluxing in benzene in the presence of TsOH. The reaction mixture after work up yielded the crude 4-cyano-5-methylthio-7-phenylbenzo[b]thiophene
7a which was purified by column chromatography using hexane/ethyl acetate as eluent to afford pure 7a as colourless crystals (m.p. 111-112 °C) in 70% yield. The compound was characterized on the basis of its analytical and spectral data as follows.

IR (KBr): v max 2208, 1645, 1558, 1483 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 2.66 (s, 3H, SCH₃), 7.34 (s, 1H, ArH), 7.47-7.60 (m, 4H, ArH), 7.68-7.71 (m, 3H, ArH).

¹³C NMR (75 MHz, CDCl₃); δ 17.10, 109.30, 116.40, 122.71, 123.13, 128.16, 129.13, 129.30, 131.52, 136.86, 138.81, 141.22, 142.32.

MS (m/z, %) 281 (M⁺, 100), 233 (M⁺- 48, 27).

Anal. Calcd. for C₁₆H₁₁NS₂ (281.40): C, 68.29; H, 3.94; N, 4.98%; Found: C, 68.70; H, 3.87; N, 5.03%.

The addition-elimination product was characterized only in this case and in the subsequent reactions. These intermediates were generally recognized by tlc spot and the crude adducts were directly subjected to cyclization reactions to afford the corresponding benzo[b]thiophenes.

Also, to generalize this simple methodology the selection of α-oxoketene dithioacetals was carefully done so that the product benzo[b]thiophenes will carry appropriate mono and di substituents including the corresponding annelated products. Also the α-oxoketene dithioacetals were suitably modified to yield 5-alkoxy and 5-amino benzo[b]thiophenes.
The thiophene-3-acetonitrile 4 was then reacted with α-oxoketene dithioacetals derived from acetone, ethyl methyl ketone, propiophenone and isopropyl methyl ketone under the similar reaction conditions as described earlier to afford the corresponding addition elimination products 6b-e in excellent yields (scheme 15). These products were subsequently cyclized in the presence of TsOH in refluxing benzene to afford the corresponding benzo[b]thiophene 7b-e in 69-72 % overall yields. All these benzo[b]thiophenes were fully characterized by their analytical and spectral data which are in accordance with the assigned structure and are recorded in the experimental section.

The synthesis of 6,7-annulated benzo[b]thiophene was next examined. It may be noted that the synthesis of 6,7-cyclopentanobenzo[b]thiophene described by Albert Padwa (scheme 10) starting from the not so easily available thiophene-3-methyl-3-carboxylic acid. There are at least four additional steps before the precursor 35 is generated. To highlight the synthesis of 6,7-cyclopentanobenzo[b]thiophene 7f (scheme 16) as against that described by Padwa and co-workers, we have reacted commercially available thiophene-3-acetonitrile with cyclopentanone mercaptal 5f under the described conditions to afford the addition elimination product in good yield which was pure enough to carry out the next step. The crude 6f was treated with TsOH to afford the corresponding 6,7-cyclopentanobenzo[b]thiophene in 67 % yield. The structure of 7f was fully confirmed by its analytical and
**Scheme 15**

$$\text{CN} \quad \Theta \quad \text{MeS} \quad \text{SMe} \quad ~\text{R}_2$$

1. $\text{NaH/DMF/0 - RT}$
2. $\text{PTSA/}C_6H_6/\Delta$

<table>
<thead>
<tr>
<th>Starting Material 5</th>
<th>Product 7</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
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<tr>
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<tr>
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<tr>
<td><img src="5e.png" alt="Image" /></td>
<td><img src="7e.png" alt="Image" /></td>
<td>63</td>
</tr>
</tbody>
</table>
spectral data as given as below.

Colourless crystals; m.p. 129-130 °C (chloroform-ether); Yield 77%; IR (KBr): $v_{\text{max}}$ 2208, 1649, 1562, 1421 cm$^{-1}$;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.25 (pentet, 2H, J=7.5 Hz,), 2.52 (s, 3H, SCH$_3$), 3.11-3.47 (m, 4H, -(CH$_2$)$_r$), 7.45 (d, 1H, J=5.6 Hz,), 7.54 (d, 1H, J=5.6 Hz,);

$^{13}$C NMR (400 MHz): $\delta$ 18.81, 24,06, 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%), 230 (M$^+$-15, 47);

Anal. Calcd. for C$_{13}$H$_{11}$NS$_2$ (245.37): C, 63.64; H, 4.52; N, 5.71%; Found: C, 63.96; H, 4.59; N, 5.67%.

Similarly, various 6,7-annelated benzo[b]thiophene 7g, 7h and 7i were obtained in 62-69 % overall yields by following the sequential steps by reacting the corresponding mercaptals derived from cyclohexanone, indanone and tetralone with 4. The analytical and spectral data 7g-7i were in conformity with the assigned structures which are described in the experimental section.

In the next experiments the benzo[b]thiophene carrying amino and methoxy groups at 5-position were included. Thus the S,N-acetal 5j was reacted with 4 as described earlier and addition elimination products 6j which was obtained in about 85 % yield, was directly cyclized in the presence of
### Scheme 16

1. **Starting Material 5**
2. **Product 7**
3. **Yield %**

<table>
<thead>
<tr>
<th>Starting Material 5</th>
<th>Product 7</th>
<th>Yield %</th>
</tr>
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<tbody>
<tr>
<td>![5f]</td>
<td>![7f]</td>
<td>77</td>
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<tr>
<td>![5g]</td>
<td>![7g]</td>
<td>65</td>
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<tr>
<td>![5h]</td>
<td>![7h]</td>
<td>62</td>
</tr>
<tr>
<td>![5i]</td>
<td>![7i]</td>
<td>65</td>
</tr>
</tbody>
</table>
TsOH in refluxing benzene then the corresponding 5-pyperidine-4-cyano-7-phenylbenzo[b]thiophene 7j was obtained in 74 % yield. The structure of 7j was confirmed by its analytical and spectral which are given in the experimental section.

Similarly acetone mercaptal was treated with morpholine to obtain the corresponding S,N-acetal 5k as described earlier which was reacted with 4 under similar reaction conditions to afford the corresponding crude addition elimination product in high yield and was cyclized as described above to yield the corresponding 4-cyano-5-morpholinobenzo[b]thiophene (7k) in 76 % yield. In the next experiment 5-methoxybenzo[b]thiophene was synthesized as typical example. Thus the O,S-acetal 5l was prepared to our earlier reported method from acetophenone and reacted with 4 under similar reaction conditions to afford after work-up the corresponding addition elimination product 6l with the elimination of methylthio group. The product was then cyclized as described to afford the corresponding 4-cyano-5-methoxy-7-methylbenzo[b]thiophene (7l) in 63% yield (scheme 17). The compound 7l was characterized by spectral and analytical data which are recorded in the experimental section.
<table>
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<tr>
<th>Starting Material 5</th>
<th>Product 7</th>
<th>Yield %</th>
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<tbody>
<tr>
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<td><img src="image2" alt="Image of 7j" /></td>
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<tr>
<td><img src="image3" alt="Image of 5k" /></td>
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<tr>
<td><img src="image5" alt="Image of 5l" /></td>
<td><img src="image6" alt="Image of 7l" /></td>
<td>62</td>
</tr>
</tbody>
</table>
In the next attempt it was made to achieve the dethiomethylation on 7 with limited success. Thus when 7a was treated with W4 Raney Ni in ethanol, the reaction mixture did not yield any identifiable product. Similarly, when 7a was treated with NiCl₂/NaBH₄ in ethanol also yielded an inseparable product mixture.

Again attempts were made to achieve selective dethiomethylation by using deactivated Raney Ni. The W4 Raney Ni was deactivated described in the literature by refluxing it in acetone for 2 hours. Only 7a yielded benzo[b]thiophene in 61 % yield involving selective dethiomethylation with simultaneously following reductive alkylation of cyano group to the corresponding N,N-diethylaminomethyl functionality. Compound 43 was fully characterized by analytical and spectral data which are given in the
experimental section. However 7c failed to yield the corresponding
dethiomethylated product when it was treated with similar Raney Ni in the
presence of refluxing ethanol. On the other hand the product 7e underwent
dethiomethylation with the same Raney Ni at room temperature to yield 4-
cyano-6,7-cyclopentanobenzo[b]thiophene 44 in 55 % yield (scheme 19). It
was characterized by its analytical and spectral data which are given in the
experimental section. Under similar reaction condition 7a in methanol failed
to give any product with well defined structure.

In one of the experiments the cyano group was hydrolyzed with
ethanolic NaOH in shield tube and the product after work-up yielded the
corresponding 4-carboxylic product in 77 % yield. The product was
characterized by its spectral and analytical data which are given in the
experimental section. It is to be noted that all the benzo[b]thiophenes
described in the above schemes failed to undergo dethiomethylation under
anyone of methods described in scheme 19.

In conclusion, we have developed a new method for benzo[b]thiophene
synthesis with regiocontrolled on 4, 5, 6 and 7 positions. Substituents could be
introduced at 6 and 7 positions by carrying them through their open chain
precursors. Also by reacting with α-oxoketene dithioacetals derived from
cycloalkanones, the method can be extended to the synthesis of 6,7-annelated
benzo[b]thiophenes. The synthesis of 6,7-cyclopentanobenzo[b]thiophene
skeleton by our method is superior to the one recently described by Padwa and co-workers (scheme 10). The method is flexible for substituents at 5-position where methylthio group can be replaced by methoxy and amino groups also. However the method suffers some limitations which remain unresolved. It was not possible to knock of methylthio group selectively without effecting the thiophene ring sulphur. We are continuing to develop suitable reagent to remove selectively only the side chain sulphur and the work is in this direction is in progress.
EXPERIMENTAL

General

Thiophene-3-acetonitrile was purchased from Aldrich and used as supplied. Commercially available sodium hydride (50% suspension in mineral oil, Spectrochem, Lancaster) was used. N,N-Dimethyl formamide was distilled from calcium hydride prior to use. p-Toluene sulfonic acid was purchased from Loba Chemie and used as such. Dry benzene was obtained by keeping over calcium chloride followed by distillation and again keeping over sodium wire. The commercial samples of acetone, acetophenone, ethyl methyl ketone, cyclopentanone, cyclohexanone, acetyl acetone were purified by simple distillation. Morpholine and piperidine were distilled from sodium hydroxide. Propiophenone, 1-indanone, 1-tetralone, were prepared according to the reported procedure. Dimethyl trithiocarbonate was prepared by according to the literature procedure. Oxoketene-S,S-acetals, and -N,S-acetals were prepared according to the earlier reported procedures and the general procedures are given in the experimental section of Chapter II.


To a stirring suspension of sodium hydride (10 mmol) in dimethyl formamide (10 ml) at 0°C, a solution of thiophene-3-acetonitrile (5 mmol) in dimethyl formamide (5 ml) was added dropwise. After 15 minutes, the appropriate α-oxoketene acetal (5 mmol) in dimethylformamide (10 ml) was
slowly added and the reaction mixture was allowed to warm to room temperature with stirring during 8-10 hours. It was poured into saturated ammonium chloride solution (200 ml) and extracted with chloroform (3x50 ml). The combined organic extracts were washed with water (3x100 ml), dried over anhydrous sodium sulfate and evaporated to give the crude 1,4-adducts. The addition-elimination obtained by the reaction of thiophene-3-acetonitrile and oxoketene dithioacetal was purified by passing through silica gel column using hexane-ethyl acetate (97:3) and characterized 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-toluenesulphonic acid (10 mmol) was added and the reaction mixture was refluxed with stirring for 3-4 hours. 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 (2x100 ml), dried over anhydrous sodium sulfate and evaporated to give crude benzo[b]thiophene which was purified by column chromatography (silica gel) using hexane-ethylacetate (97:3) as eluent.

7-Cyano-4-methyl-6-(methylthio)benzo[b]thiophene (7b).

Colourless crystals; m.p. 150-151° C (chloroform-ether); Yield 70%; IR (KBr): $\nu_{\text{max}}$ 2208, 1649, 1562, 1421 cm$^{-1}$. 
1H NMR (300 MHz, CDCl$_3$): δ 2.62 (s, 3H), 2.63 (s, 3H, CH$_3$), 7.15 (s, 1H, ArH), 7.53 (d, 1H, $J$ = 6.0 Hz), 7.65 (d, 1H, $J$ = 6.1 Hz);
MS (m/z, %) 219 (M$^+$, 100%), 204 (M$^+$-15, 32);
Anal. Calcd. for C$_{11}$H$_9$NS$_2$ (219.33): C, 60.24; H, 4.14; N, 6.29%; Found: C, 60.43; H, 4.15; N, 6.26%.

7-Cyano-4,5-dimethyl-6-(methylthio)benzo[b]thiophene (7c).

Colourless crystals; m.p. 123-125 °C (chloroform-ether); Yield 64%;
IR (KBr): $\nu_{\text{max}}$ 2205, 1470, 1440 cm$^{-1}$;
1H NMR (400 MHz, CDCl$_3$): δ 2.46 (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 2.60 (s, 3H, SCH$_3$), 7.51 (d, 1H, $J$=5.6 Hz), 7.55 (d, 1H, $J$=5.5 Hz);
13C NMR (100 MHz): δ 17.56, 19.78, 19.95, 111.19, 117.41, 123.35, 128.94, 135.84, 135.99, 137.63, 139.33, 141.72;
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, 4.76; N, 6.02%.

4-Cyano-6-methyl-5-(methylthio)-7-phenylbenzo[b]thiophene (7d)

Colourless crystals; m.p. 122-123 °C (chloroform-hexane); Yield 76%;
IR (KBr): $\nu_{\text{max}}$ 2209, 1535, 1447 cm$^{-1}$
1H NMR (400 MHz, CDCl$_3$): δ 2.47 (s, 3H, CH$_3$), 2.54 (s, 3H, SMe), 7.32 (d, 1H, $J$=1.6 Hz), 7.47-7.52 (m, 3H, Ar), 7.54-7.55 (m, 2H, ArH);
13C NMR (100 MHz, CDCl$_3$): δ 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), 247 (M⁺-48, 69);

Anal. Calcd. for C₁₇H₁₃NS₂ (295.42): C, 69.12, H, 4.43, N, 4.74 %; Found: C, 69.35; H, 4.21; N, 4.90 %.

4-Cyano-6-isopropyl-5-(methylthio)benzo[b]thiophene (7e)

Yellow crystals; m.p. 56-57 °C (chloroform-ether); Yield 63%.

IR (KBr): νmax 2208, 1651, 1546 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.41 (d, 6H, J = 6.8 Hz, (CH₃)₂), 2.64 (s, 3H, SMe), 3.24-3.27 (m, 1H, CH), 7.24 (s, 1H, ArH), 7.47 (d, 1H, J = 4.8 Hz, ArH), 7.61 (d, 1H, 5Hz)

¹³C NMR (100 MHz, CDCl₃): δ 17.23, 22.29, 33.96, 104.36, 116.49, 119.78, 122.64, 122.92, 128.19, 128.48, 130.02, 136.84, 140.93, 141.68, 148.08.

MS (m/z, %) 247 (M⁺, 100), 232 (M⁺-15, 83.4)

Anal. Calcd. for C₁₉H₂₁NS₂ (295.44): C, 77.24, H, 7.16, N, 4.74 %; Found: C, 77.01; H, 7.31; N, 4.53 %.

4-Cyano-5-methylthio-6,7,8,9-tetrahydronaphtho[2,1-b]thiophene (7g).

Colourless crystals; m.p. 131-132 (C (chloroform-ether); Yield 65%;

IR (KBr) νmax 2205, 1525, 1440 cm⁻¹;

¹H NMR (300 MHz, CDCl₃): δ 1.91-1.93 (m, 4H, -(CH₂)₂), 2.48 (s, 3H, SCH₃), 2.93-2.95 (m,2H, -CH₂⁻), 3.07-3.08 (m, 2H, -CH₂⁻), 7.50 (d, 1H, J=5.6 Hz), 7.53 (d, 1H, J=5.5 Hz).

¹³C NMR (100 MHz): δ 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 (M⁺-25, 100)

Anal. Calcd. for C₁₄H₁₃NS₂ (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)fluoreno[3,4-b]thiophene (7h).

Colourless crystals; m.p. 214-215°C (chloroform-ether); Yield 62%; IR (KBr):

\( v_{\text{max}} \) 2210, 1567, 1470 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.59 (s, 3H, SMe), 3.92 (s, 2H, -CH₂-), 7.38-7.46 (m, 2H, ArH), 7.54 (d, 2H, \( J=4.5 \) Hz, ArH), 7.63 (d, 1H, \( J=5.2 \) Hz, ArH), 7.79 (d, 1H, \( J=6.0 \) Hz, ArH).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 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 C₁₇H₁₁NS₂ (293.41): C, 69.59; H, 3.78; N, 4.77%; Found: C, 69.21; H, 3.70; N, 4.71%.

4-Cyano-6,7-dihydro-5-(methylthio)phenanthreno[3,4-b]thiophene (7i).

Colourless crystals; m.p. 122-123 °C (chloroform-ether); Yield 65%;

IR (KBr): \( v_{\text{max}} \) 2210, 1567, 1470 cm\(^{-1}\);

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 2.48 (s, 3H, SMe), 2.84 (t, 2H, \( J = 6.8 \) Hz, -CH₂-), 3.30 (t, 2H, \( J = 6.8 \) Hz, -CH₂-), 7.25-7.45 (m, 3H, ArH), 7.61-7.66 (m, 3H, ArH), 7.61-7.66 (m, 2H, ArH), 8.27(d; 1H, \( J = 7.6 \) Hz, ArH).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 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 (M^+-48, 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-7-phenyl-5-piperidinobenzo[b]thiophene (7j).

Colourless crystals; m.p. 141-142 °C (chloroform-ether); Yield 75%;

IR (KBr): \nu_{\text{max}} 2212, 1565 cm^{-1};

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \delta 1.62-1.63 (m, 2H, -CH\textsubscript{2}r), 1.80-1.81 (m, 4H, -(CH\textsubscript{2})\textsubscript{r}), 3.30-3.32 (m, 4H, -N(CH\textsubscript{2})\textsubscript{r}), 7.00 (s, 1H, ArH), 7.29 (s, 2H, ArH), 7.44-7.51 (m, 5H, ArH).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \delta 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\textsubscript{20}H\textsubscript{18}N\textsubscript{2}S (318.44): C, 75.44; H, 5.70; N, 8.80%; Found: C, 75.86; H, 5.77; N, 8.73%.

4-Cyano-7-methyl-5-morpholinoberizo(b]thiophene (7k).

Colourless crystals; m.p. 91-92 °C (chloroform-ether); Yield 68%;

IR (KBr): \nu_{\text{max}} 2201, 1579 cm^{-1};

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \delta 2.63 (s, 3H, CH\textsubscript{3}), 3.27 (t, 4H, J = 4.4 Hz, -(CH\textsubscript{2})\textsubscript{r}), 3.91 (t, 4H, J = 4.4 Hz, O(CH\textsubscript{2})\textsubscript{2r}), 6.84 (s, 1H, ArH), 7.30 (d, 1H, J = 5.2 Hz, ArH), 7.36 (d, 1H, J = 5.2 Hz, ArH).
$^{13}$C NMR (100 MHz): δ 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$_2$O$_S$ (258.34): C, 65.09; H, 5.46; N, 10.84%; Found: C, 65.37; H, 5.67, N, 10.61%.

4-Cyano-5-ethyl(diethylamine)-7-phenylbenzo[b]thiophene (43)

Yellow crystals; m.p. 71-72 °C (chloroform-ether); Yield 68%;

IR (KBr): $\nu_{\text{max}}$ 2900, 1650, 1600, 1550 cm$^{-1}$;

$^1$H NMR (400 MHz, CDCl$_3$): δ 1.07 (t, 6H, 2XCH$_3$), 2.61 (q, 4H, -CH$_2$-), 3.92 (s, 2H, -CH$_2$), 7.31-7.50 (m, 6H, ArH), 7.71 (m, 8H, ArH).

MS (m/z, %) 295 (M⁺, 52%), 223 (M⁺-72, 100)

Anal. Calcd. for C$_{19}$H$_{21}$NS (295.44): C, 77.24; H, 7.16; N, 4.74%; Found: C, 75.40; H, 7.29, N, 4.56%.

5-Methylthio-7-phenylbenzo[b]thiophene-4-carboxylic acid (45)

Colourless crystals; m.p. 121-122 °C; Yield 77 %;

IR (KBr): $\nu_{\text{max}}$ 3354, 2226, 1743, 1644 cm$^{-1}$;

$^1$H NMR (400 MHz, CDCl$_3$): δ 2.49 (s, 3H, SCH$_3$), 7.32 – 7.34 (m, 2H, ArH), 7.39-7.43 (m, 1H, ArH), 7.46 – 7.50 (m, 2H, ArH), 7.62 – 7.71 (m, 2H, ArH), 7.88 (brs, 1H, OH).

Anal. Calcd. for C$_{16}$H$_{12}$S$_2$O$_3$ (316.45): C, 60.75; H, 4.16; Found: C, 60.40; H, 4.29%.
4-Cyanoindano[5,4-b]thiophene (44).

Colourless crystals; m.p. 101-102 °C (chloroform-ether); Yield 55%;

IR (KBr): $\nu_{\text{max}}$ 2200, 1579 cm$^{-1}$;

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.26-2.31 (m, 2H, -CH$_2$), 3.08 (m, 4H, -(CH$_2$)$_2$), 7.55-7.75 (m, 3H, ArH).

MS (m/z, %) 199 (M$^+$, 100%);

Anal. Calcd. for C$_{12}$H$_9$NS (199.34): C, 65.09; H, 5.46; N, 10.84%; Found: C, 65.37; H, 5.67, N, 10.61%.
REFERENCES


