Studies in sulfur heterocycles. Part 12.[1] Use of 5,6-dihydrobenzo[*b*]-thiophen-7(4*H*)-one in the synthesis of condensed sulfur heterocycles

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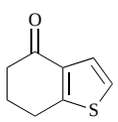
Readily available 5,6-dihydrobenzo[*b*]thiophen-7(4*H*)-one has been used as a convenient intermediate for the synthesis of several condensed heterocyclic systems and substituted benzo[*b*]thiophenes.

Functionalised benzo[*b*]thiophene (fully aromatic or partially hydrogenated) is important as a substrate for various annelations leading to polynuclear compounds incorporating fused thiophene rings. Such compounds have been investigated as potential chemical carcinogens,[2] as analogues of naturally occurring bio-active molecules[3,6] or as heterohelicenes.[7] Reported syntheses[8,9] of 6- and 7-substituted benzo[*b*]thiophenes are fewer than of those of compounds substituted in other positions; this reflects the relative difficulty in preparing the former. 6,7-Dihydrobenzo[*b*]thiophen-4(5*H*)one **1** has been much used[8] for the convenient preparation[9] of substituted benzo[*b*]thiophenes in contrast to 5,6-dihydrobenzo[*b*]thiophen-7(4*H*)-one **2** which has not been so used, presumably because of its inaccessability.[10–12]



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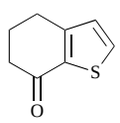
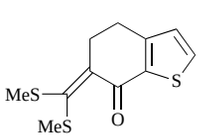


2

We recently reported[1] a simple, short high-yielding synthesis of **2** from a commercially available starting material and demonstrated its potential as a synthetic intermediate for sulfur heterocycles. We report herein an extension of this work to several condensed sulfur–nitrogen heterocycles and its conversion into 6- and 7-substituted benzo[*b*]thiophenes which are accessible only with difficulty by conventional means.

Results and discussion

The ketone **2** is readily converted in near quantitative yield into 6-bis(methylsulfanyl)methylidene-5,6-dihydrobenzo[*b*]thiophene-7(4*H*)-one **3** which acts as a versatile intermediate in the annelations reported below. Thus **2** was treated with iodomethane in dry acetone in the presence of anhydrous potassium carbonate to give the β-oxo dithioester **4**[1] which was then converted into **3**.[1]



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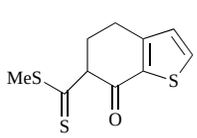
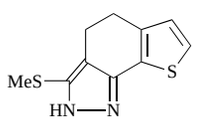


4

The 1,3-electrophilic centres in **3** upon reaction with suitable bifunctional nucleophiles result in the annelation[10] of a third five- or six-membered nitrogen heterocycles onto the existing benzo[*b*]thiophene core. Thus, reaction of hydrazine hydrate with **3** in refluxing ethanol gives, by cyclisation with simultaneous expulsion of methanethiol, the fused pyrazole **5** (70%).



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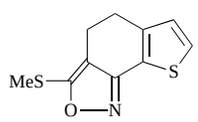
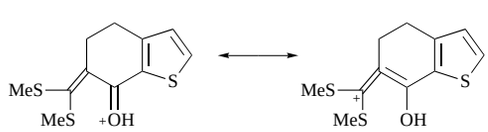


6

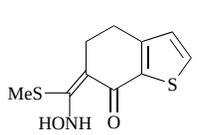
Reaction of **3** with hydroxylamine, an asymmetric bifunctional nucleophile, gives two regioisomeric fused isoxazoles, the nature of the product depending upon the reaction conditions. The electrophilicities of the 1,3-carbon centres of **3** and, consequently, the regiocontrol in its reaction with hydroxylamine are governed by the pH of the reaction medium.[13] Under basic conditions in the presence of methanolic sodium methoxide, the intermediate oxime cyclises to give 3-methylsulfanyl-4,5-dihydrothieno[3,2-*g*]-2,1-benzisoxazole **6** with the expulsion of methanethiol. Initial protonation of **3** takes place when the reaction conditions are acidic, the protonated species **7** being stabilised by charge delocalisation. Subsequent nucleophilic attack by hydroxylamine at the positive charge centre in **7b** and



7a **7b**

concomitant expulsion of methanethiol affords the intermediate **8** which finally cyclises to the regioisomeric 3-methylsulfanyl-4,5-dihydrothieno[3,2-*g*]-1,2-benzisoxazole **9**.

In the presence of refluxing methanolic sodium methoxide, guanidine liberated from its hydrochloride reacts with **3** to afford 2-amino-4-methoxy-5,6-dihydrothieno[3,2-*h*]quinazoline **10** (70%). Besides releasing the free guanidine from its salt,



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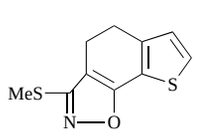
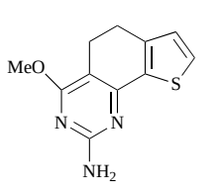


9

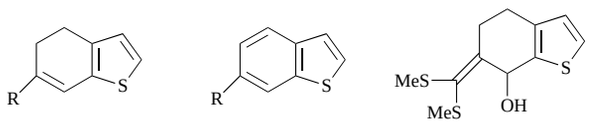


10

sodium methoxide acts as the cyclising agent and converts the free methylsulfanyl group into methoxide after cyclisation.

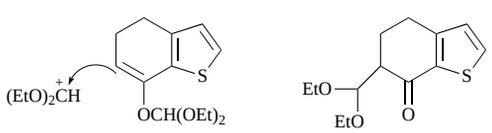
As stated above, 6- and 7-substituted benzo[*b*]thiophenes are relatively difficult to obtain by known methods. The α-oxo ketene dithioacetal **3** or its precursor ketone **2**, however, provided convenient access to methyl 4,5-dihydrobenzo[*b*]-thiophene-6-carboxylate **11** and the corresponding aldehyde **12** which could be aromatised to **13** and **14**. Thus, chemoselective 1,2-reduction of **3** with sodium borohydride following the

methodology developed by Saquet and Thuillier[14] afforded the acid-sensitive alcohol **15**, the excellent selectivity arising no



11 R = CO_2Me
12 R = CHO
13 R = CO_2Me
14 R = CHO
15

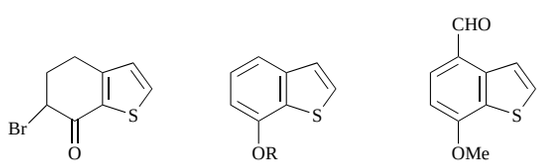
doubt from the alkylthio groups as propounded earlier by Ireland and Marshall.[15,16] Even though the carbinol was insufficiently stable to undergo the purification necessary to prepare an analytical sample, it was sufficiently pure for the subsequent steps and could be characterised spectroscopically. The presence of the hydroxy function was characterised by IR absorption at 3350 cm^{-1} and a ^1H NMR signal at δ 7.50 (1H, br s); other signals supported the structural assignment: δ_H 6.9 and 6.8 (both d, thiophene H), δ_H 2.5 and 2.3 (MeS) and δ_H 5.70 (7-H). The alcohol upon treatment with boron trifluoride–diethyl ether and methanol, following the methodology developed by Junjappa and *et al.*[17] underwent a 1,3-carbonyl transposition to afford the dihydro ester **11** which was aromatised with DDQ in hot 1,4-dioxane to give the ester **13**. Similarly, **15** when heated with dimethyl sulfoxide[18] gave the dihydro aldehyde **12** and was then aromatised to the aldehyde, **14**, but in only mediocre yield; it was accompanied by an unidentifiable decomposition product. Better access to **12** from **2** was achieved using Suzuki's methodology;[19,20] in this, the latter was treated first with triethyl orthoformate in the presence of boron trifluoride–diethyl ether and then by diisopropylethyl amine. It is believed[9] that the process consists of initial *O*-alkylation with the species $^+CH(OEt)_2$ followed by attack on the resulting enol ether **16** by a second diethoxycarbonium ion to afford the keto acetal **17**. Boro-



16 **17**

hydride reduction of the latter and spontaneous dehydration of the resulting carbinol acetal during acidic work-up afforded the dihydro aldehyde **12** in good yield and free of any undesired side-product.

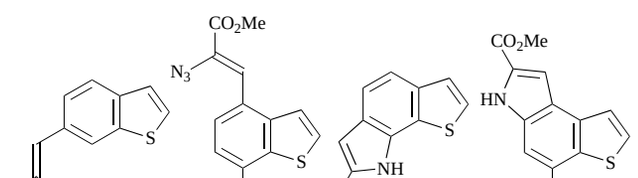
A hydroxy group in the 7-position of benzo[*b*]thiophene molecule would provide a convenient 'handle' for annelating a five-,[21] six-[21,22] or seven-membered[23] oxygen heterocycle in the same way as we have earlier obtained similar compounds from 4-hydroxybenzaldehyde. However, barring only one example[24] no such use of 7-hydroxybenzo[*b*]thiophene **18** is on record presumably because most of the methods of synthesis[24–26] of **18** which are reported in the literature fail to provide easy access to this compound. Of all these methods only the recently reported one by Rahman and Scrowston[26] is relatively convenient and affords the compound in a reasonable yield. The bromo ketone



19
18 R = H
20 R = Me
21 R = $CH_2{=}CHCH_2$
22 R = $CH_2C{\equiv}CH$
23

19 obtained from **2** as reported earlier[1] was converted into **18** using lithium bromide, lithium carbonate and dimethylformamide[27] in very good yield (80%). *O*-Alkylation of **18** was facile. 7-Methoxy-[25] **20** and 7-allyloxy[26] benzo[*b*]thiophene **21** have been reported earlier, the former being found by earlier workers to be difficult to purify. The hydroxy compound was *O*-alkylated with methyl iodide, and prop-2-ynyl bromide to afford 7-methoxy **20** and 7-prop-2-ynyloxy **22** benzo[*b*]thiophene, respectively. Compounds **21** and **22** can serve as substrates for annelations which would lead to tricyclic compounds having a five- or six-membered oxygen heterocycle angularly fused to a benzo[*b*]thiophene molecule *via* Claisen rearrangement–cyclisation protocol. Work is in progress in that direction.

Among the products resulting from annelating nitrogen heterocycles to benzo[*b*]thiophene core, thienoindoles, being analogues of biologically important naturally occurring pyroloindoles,[6] *viz* PDE I and PDE II, constitute an interesting class of compounds. Several synthesis[6,28] of such analogues have been reported. We report here synthesis of two thienoindoles which could be obtained in good yield using only a few steps and simple reactions. The methodology used for the purpose was the thermolysis of vinyl azide, which can be readily obtained from aromatic aldehydes and alkyl azidoacetate followed by nitrene insertion, as developed earlier by Rees and co-workers[29] and which we have earlier successfully used for synthesizing thieno[2,3-*g*]indole.[9] The aldehydes used for this purpose were benzo[*b*]thiophene-6-carbaldehyde **14** and 7-methoxybenzo[*b*]thiophene-4-carbaldehyde **23** which could be obtained from 7-methoxybenzo[*b*]thiophene **20** by Vilsmeier–Haack formylation. The aldehydes underwent smooth condensation with methyl azidoacetate in the presence of methanolic sodium methoxide at −15 °C to afford the vinyl azides **24** and **25** sufficiently pure for the next step. The thienoindoles **26** and **27** could be obtained upon refluxing the vinyl azides in xylene for 3 h. Compounds **24**–**27** displayed all the expected features in their IR and ^1H NMR spectra. The H-3 in both the thienoindoles showed some broadening when their 60 MHz NMR spectra were recorded. In 200 and 300 MHz spectra a distinct coupling of *J* 2 Hz were noticed. That this coupling was with the NH proton which gave a typical broad one-proton singlet was obvious when H-3 signal collapsed into a singlet and the NH signal disappeared upon shaking with D_2O. Our attempts to hydrolyse and decarboxylate the ester function in **26** and **27**



24 **25** **26** **27**

were frustrated and resulted in every case in the formation of uncharacterisable polymeric materials. The other alternative is to convert the ester function into aldehyde for eventual decarboxylation. This pathway towards the sulfur analogues of PDE I and PDE II is currently receiving our attention and will be reported later.

Experimental

Melting points (uncorrected) were reported in open capillaries on a hot-stage apparatus. Commercially available solvents were distilled prior to use. IR spectra were recorded on a Perkin–Elmer 298 spectrometer, for solids in potassium bromide discs and for liquids by placing a thin layer of the sample between two potassium bromide discs. ^1H NMR were recorded in carbon tetrachloride solution unless otherwise stated on a Varian EM 360 or JEOL FX-100 spectrometer. Chemical shifts are expressed in terms of δ, using tetramethylsilane as internal standard. Anhydrous sodium sulfate was used as drying agent. Light petroleum boiled in the range 60–80 °C.

6-Bis(methylsulfanyl)methylidene-5,6-dihydrobenzo[*b*]thiophene-7(4*H*)-one 3

Potassium carbonate (1.4 g, 10.6 mmol) was added to a solution of **4**[1] in dry acetone (100 ml). After being refluxed for 3 h, the reaction mixture was cooled to 0 °C and treated with methyl iodide (1.5 g, 10.6 mmol) in dry acetone (20 ml), added dropwise at that temperature whilst being magnetically stirred. The stirring was continued for 2 h at 0 °C and then for 10 h at room temperature. After this period the reaction mixture was filtered and evaporated under reduced pressure and the residue was poured into crushed ice. The resulting mixture was extracted with chloroform, and the extract was washed with water, dried and evaporated. The residue was purified by passage through a short column of silica gel, using light petroleum–ethyl acetate (9:1) as eluent to afford **3** as yellow crystals (1.4 g, 94%), mp 62–64 °C (Found: C, 51.75; H, 4.91. $C_{11}H_{12}OS_3$ requires C, 51.52; H, 4.72%); ν_{max}/cm^{-1} 1620 (CO); δ_H 7.5 (d, 1H, H-3, *J* 5), 7.0 (d, 1H, H-2, *J* 5), 3.5–2.8 (m, 4H, H-4 and H-5), 2.4 (s, 3H, SMe) and 2.3 (s, 1H, SMe).

3-Methylsulfanyl-4,5-dihydro-2*H*-thieno[3,2-*g*]indazole 5

Compound **3** (256 mg, 1 mmol) together with hydrazine hydrate (1 mol equiv.) was refluxed in ethanol (3 ml) for 8 h after which solvent removal under reduced pressure and trituration of the residue with hexane afforded a yellow solid which was crystallised from hexane–benzene to afford **5** (170 mg, 70%); mp 211–212 °C (Found: C, 54.06; H, 4.23 N, 12.21. $C_{10}H_{10}N_2S_2$ requires C, 54.02; H, 4.53 N, 12.06%); ν_{max}/cm^{-1} 3020 (NH); δ_H([$^2H_6$]-DMSO) 13.6 (1H, br s, NH), 7.3 (1H, d, H-6, *J* 5), 7.1 (1H, d, H-7, *J* 5), 3.44–3.12 (4H, CH_2) and 3.12 (s, 3H, SMe); *m*/*z* (EI) 222 (M^+) and 175.

3-Methylsulfanyl-4,5-dihydrothieno[2,3-*g*]-2,1-benzisoxazole 6

Hydroxylamine hydrochloride (222 mg, 3.2 mmol) was added to a magnetically stirred solution of sodium methoxide, prepared from sodium (92 mg, 4 mmol) in dry methanol (16 ml). After being stirred for further 15 min, the mixture was treated with **3** (200 mg, 0.8 mmol) and then refluxed for 14 h. After this, the mixture was evaporated, treated with ice-cold water (25 ml) and extracted with ether. The extract was dried and evaporated to afford a crude product which was chromatographed over silica gel (eluent light petroleum–ethyl acetate, 9:1) to give **6** as a light yellow oil (130 mg, 74%) (Found: C, 54.18; H, 4.19; N, 6.54. $C_{10}H_9NOS_2$ requires C, 53.84; H, 4.03; N, 6.27%); δ_H($CDCl_3$) 7.3 (1H, d, H-6, *J* 5), 6.9 (1H, d, H-7, *J* 5), 2.9–2.7 (4H, m, CH_2) and 2.6 (3H, s, SMe); *m*/*z* (EI) 223 (M^+), 180, 148 and 122.

3-Methylsulfanyl-4,5-dihydrothieno[3,2-*g*]-2,1-benzisoxazole 9

Sodium acetate (222 mg, 3.2 mmol), acetic acid (8 ml) and a solution of hydroxylamine hydrochloride (222 mg, 3.2 mmol) in water (4 ml) were added to **3** (200 mg, 0.8 mmol) dissolved in benzene (8 ml). After being made homogenous by addition of ethanol (8 ml) the reaction mixture was refluxed for 16 h. It was then evaporated under reduced pressure and the mixture was extracted with dichloromethane. The extract was washed with water, dried and evaporated. Chromatography of the residue on a short column of neutral alumina afforded **9** as a light coloured crystalline material (140 mg, 70%); mp 52–53 °C (Found: C, 53.89; H, 4.22; N, 6.10. $C_{10}H_9NOS_2$ requires C, 53.81; H, 4.03; N, 6.27%); δ_H 7.2 (1H, d, H-6, *J* 5), 6.9 (1H, d, H-7, *J* 5), 2.9–2.6 (m, 4H, CH_2) and 2.6 (3H, s, SMe); *m*/*z* (EI) 223 (M^+), 208, 177 and 148.

2-Amino-4-methoxy-5,6-dihydrothieno[3,2-*h*]quinazoline 10

Guanidine hydrochloride (96 mg, 1 mmol) and **3** (256 mg, 1 mmol) were added to a solution of sodium methoxide, prepared from sodium (50 mg, 2 mmol) in dry methanol (10 ml) and the mixture was refluxed for 8 h. After this, solvent removal from the mixture by distillation left a residue which was triturated with water to give **10** as a white crystalline material (180 mg, 70%); mp 204–205 (Found: C, 56.67; H, 4.78; N, 18.17. $C_{11}H_{11}ON_3S$ requires C, 56.63; H, 4.75; N, 18.21%); ν_{max}/cm^{-1} 3200 (NH) and 1650 (CN); δ_H 7.4 (1H, d, H-7, *J* 6), 7.0 (1H, d, H-8, *J* 6), 4.9 (2H, s, NH_2), 3.9 (s, 3H, OMe) and 2.9–2.8 (m, 4H, CH_2); *m*/*z* (EI) 233 (M^+).

Methyl 4,5-dihydrobenzo[*b*]thiophene-6-carboxylate 11

Sodium borohydride (100 mg, 3 mmol) was added to a solution of **3** (256 mg, 1 mmol) in dry ethanol (10 ml) which was cooled externally (ice-bath). After being stirred overnight at room temperature, the mixture was concentrated by solvent removal under reduced pressure and the residue was added to ice-cold water (50 ml), and extracted with ether (3 × 25 ml). The extract was washed with water, dried and evaporated to leave the carbinol **15** as a light yellow oil (230 mg, 89%) which was used for the subsequent step without further purification.

A solution of the above carbinol in methanol (5 ml) and boron trifluoride–diethyl ether (0.4 ml) was refluxed for 7 h. After cooling, the reaction mixture was poured into saturated aqueous sodium hydrogen carbonate and extracted with diethyl ether. The extract was thoroughly washed with water, after which solvent was distilled off to leave a crude product which was purified by chromatography over silica gel (eluent light petroleum–ethyl acetate, 9:1) to afford **11** as a light coloured oil (140 mg, 72%) (Found: C, 60.84; H, 5.17. $C_{10}H_{10}O_2S$ requires C, 61.84; H, 5.19%); ν_{max}/cm^{-1} 1720 (CO_2Me); δ_H 7.50 (1H, s, CH=), 7.25 (1H, d, H-3, *J* 5), 6.9 (1H, d, H-2, *J* 5), 3.75 (3H, s, OMe) and 2.9–2.6 (m, 4H, CH_2).

Methyl benzo[*b*]thiophene-6-carboxylate 13

A solution of **11** (140 mg, 0.72 mmol) in dry 1,4-dioxane (15 ml) was added to a warm magnetically stirred solution of DDQ (170 mg, 0.72 mmol) in the same solvent (15 ml) after which the reaction mixture was stirred and refluxed for 2 h under anhydrous conditions. After cooling, the mixture was filtered to remove the solid material and the filtrate was evaporated to leave a brown residue. This was purified by chromatography over silica gel (eluent, light petroleum–ethyl acetate, 9:1) to afford **13** as an analytically pure white solid (110 mg, 79%); mp 66–68 °C (Found: C, 62.21; H, 4.34. $C_{10}H_8O_2S$ requires C, 62.42; H, 4.20%); ν_{max}/cm^{-1} 1710 (CO_2Me); δ_H($CDCl_3$) 8.64 (1H, s, H-7), 8.12 (1H, dd, H-5, *J* 2 and 8), 7.88 (1H, d, H-4, *J* 8), 7.65 (1H, d, H-3, *J* 6), 7.45 (1H, d, H-2, *J* 6) and 4.0 (3H, s, OMe).

4,5-Dihydrobenzo[*b*]thiophene-6-carbaldehyde 12

Method A. The alcohol **15** (700 mg, 3 mmol) and dimethyl sulfoxide (1.4 ml) were heated for 5 h at 160 °C. After cooling, the mixture was treated with saturated aqueous ammonium chloride and extracted with diethyl ether. The extract was washed with water, dried and evaporated. Chromatography of the crude material over silica gel (eluent, light petroleum) afforded **12** as a light pink oil (180 mg, 44%) (Found: C, 65.94; H, 4.98. C_9H_8OS requires C, 65.84; H, 4.92%); ν_{max}/cm^{-1} 1665; δ_H 9.66 (1H, s, CHO), 7.30 (1H, s, H-7), 7.5 (1H, d, H-3, *J* 5), 7.06 (1H, d, H-2, *J* 5) and 3.06–2.75 (4H, m, CH_2).

Method B. A solution of freshly distilled boron trifluoride–diethyl ether (6.15 ml, 50 mmol) in dry methylene dichloride (8 ml) was added dropwise to stirred and freshly distilled triethyl orthoformate (6.65 mg, 40 mmol) at −30 °C under nitrogen. The mixture was then allowed to warm to 0 °C, at which temperature stirring was continued for 15 min. After the mixture had been cooled to −78 °C, a solution of **2** (304 mg, 2 mmol) in methylene dichloride (7 ml) was added to it followed by *N*,*N*-diisopropylethylamine (10.45 ml, 60 mmol) added dropwise over a period of 10 min, with continued stirring. After being stirred at −10 to −20 °C for 2 h, the resulting mixture was poured rapidly into saturated aqueous sodium hydrogen carbonate (50 ml) and then diluted with more methylene

dichloride. Stirring was continued at room temperature for 20 min, after which the organic phase was separated and washed first with cold dilute sulfuric acid (2%, v/v) and then by water. It was then dried and evaporated to leave a dark red viscous oil **17** (457 mg, 90%); ν_{max}/cm^{-1} 1670 (C=O).

The keto acetal **17** was then converted into the α,β-unsaturated aldehyde **12** in the following method.

To a well stirred solution of the acetal **17** (500 mg, 2 mmol) in absolute alcohol (10 ml) was added an excess of sodium borohydride (400 mg, 8 mmol). The mixture was stirred for 12 h after which it was decomposed with ice-cold 6 M hydrochloric acid, stirred for 3 h, diluted with water and extracted with methylene dichloride (2 × 75 ml). The combined extracts were washed with saturated brine, dried and evaporated to give the aldehyde **12** (300 mg, 91%) as a light pink oil. The compound was identical in all respects with that prepared by Method A.

Benzo[*b*]thiophene-6-carbaldehyde 14

The α,β-unsaturated aldehyde **12** (300 mg, 1.92 mmol) was aromatised with DDQ in dry 1,4-dioxane in a similar fashion to the α,β-unsaturated ester **11**. The crude reaction product was purified by chromatography over silica gel using light petroleum–ethyl acetate (95 : 5) as eluent to afford analytically pure **14** as a thick viscous material (210 mg, 70%) (Found: C, 66.58; H, 4.02. C_9H_6OS requires C, 66.66; H, 3.71%); ν_{max}/cm^{-1} 1690 (CHO); δ_H($CDCl_3$) 10.2 (s, 1H, CHO), 8.56 (1H, s, H-7), 8.04–8.00) (2H, d, H-2 and H-3, *J* 2), 7.9 (1H, d, H-4, *J* 7) and 7.84 (1H, dd, H-5, *J* 2 and 7).

7-Hydroxybenzo[*b*]thiophene 18

A solution of the bromo ketone **19**[1] (0.924 g, 4 mmol) in dry dimethylformamide (20 ml) containing a mixture of lithium bromide (0.8 g, 9 mmol) and lithium carbonate (0.6 g, 8 mmol) was refluxed under a nitrogen atmosphere for 3 h. After this, the solvent was distilled off under reduced pressure from the mixture, and the residue was treated with ice-cold water followed by ice-cold dilute hydrochloric acid. The separated gummy product was extracted with water and then by 10% aqueous sodium hydroxide. The alkali extract was acidified and extracted with ether. The organic phase was washed with water, dried and evaporated to afford crude **18** as a dark brown semi-solid which was purified by short-path distillation; bp 70 °C/0.01 mmHg to give a white solid (480 mg, 80%); mp 68 °C (lit.,[26] 68.5–69.6 °C); ν_{max}/cm^{-1} 3350 (OH); δ_H 7.40–7.46 (m, 4H, H-2, H-3, H-4 and H-5) and 6.66 (dd, 1H, H-6, *J* 7 and 2).

7-Methoxybenzo[*b*]thiophene 20

Iodomethane (250 mg, 2 mmol) was added to a solution of **18** (150 mg, 1 mmol) in dry acetone (10 ml) containing anhydrous potassium carbonate (150 mg, 1.086 mmol). After being refluxed for 8 h, the reaction mixture was filtered and the filtrate was concentrated on a water bath. After cooling, the residue was treated with cold water and extracted with diethyl ether. The extract was dried and evaporated to leave an oil **20** which was purified by short-path distillation (160 mg, 97%); bp 85 °C/0.1 mmHg (Found: C, 65.66; H, 5.07. C_9H_8OS requires C, 65.85; H, 4.91%); δ_H 7.39–7.03 (m, 4H, H-2, H-3, H-4, H-5), 6.63 (dd, 1H, H-6, *J* 6 and 2) and 3.92 (s, 3H, OMe).

7-Prop-2-ynyloxybenzo[*b*]thiophene 22

This was similarly obtained as an oil (160 mg, 85%), bp 70 °C/0.05 mmHg from **18** (150 mg, 1 mmol) and prop-2-ynyl bromide (120 mg, 1 mmol) (Found: C, 70.30; H, 4.07. $C_{11}H_8OS$ requires C, 70.33; H, 4.29%); δ_H 7.43–7.16 (m, 4H, H-2, H-3, H-4, H-5), 6.82 (dd 1H, H-6, *J* 7 and 2), 4.82 (d, 2H, OCH_2, *J* 2.5) and 2.39 (t, 1H, ≡CH, *J* 2.5).

7-Methoxybenzo[*b*]thiophene-4-carbaldehyde 23

Freshly distilled phosphorous oxychloride (275 mg, 18 mmol) was added dropwise with stirring and cooling to dry *N*,*N*-dimethylformamide (295 mg, 4 mmol) at such a rate that temperature did not exceed 5 °C. After 30 min, 7-methoxybenzo[*b*]thiophene (164 mg, 1 mmol) with few drops of *N*,*N*-dimethylformamide was added dropwise to the resulting solution at 0–5 °C which was then stirred for 0.5 h at 0 °C and then at room temperature. After this, the reaction mixture was then continuously heated until a vigorous reaction ensured at 110 °C (bath temp.). After the initial reaction had subsided the mixture was heated on an oil-bath at 90 °C for 2 h. At the end of this period, the mixture was cooled, neutralised with 25% aqueous sodium acetate, with cooling, and then extracted with diethyl ether. The extract was washed with water, dried and evaporated to give the aldehyde **23** which was crystallised from diethyl ether–light petroleum (160 mg, 83%), mp 64–66 °C; ν_{max}/cm^{-1} 1670 (CH=O) (Found: C, 62.28; H, 4.22. $C_{10}H_8O_2S$ requires C, 62.5; H, 4.16%); δ_H 10.00 (1H, s, CHO), 8.24 (1H, d, H-3, *J* 5), 7.60 (1H, d, H-5, *J* 9), 7.51 (1H, d, H-2, *J* 5), 6.69 (1H, d, H-6, *J* 9) and 4.00 (s, 3H, OMe).

Methyl 2-azido-3-(6-benzo[*b*]thienyl)propenoate 24

To a solution of sodium methoxide (225 mg, 4.2 mmol) in dry methanol kept at −15 °C, was added a mixture of carbaldehyde **14** (170 mg, 1.05 mmol) and methyl azidoacetate (483 mg, 4.2 mmol). After being magnetically stirred for 2 h at −15 °C, the reaction mixture was allowed to attain room temperature at which it was stirred for 14 h. Care was taken to protect the reaction mixture from light all the time. After this period, the reaction mixture was poured into aqueous ammonium chloride and extracted with diethyl ether. After being washed with saturated sodium bisulfite and water, the organic phase was dried and evaporated. Chromatography of the residue over silica gel (eluent light petroleum–ethyl acetate, 95 : 5) afforded **24** as light-yellow crystalline material which was recrystallised from chloroform–light petroleum (150 mg, 51%), mp 56–58 °C; ν_{max}/cm^{-1} 2120 (C=N) and 1700 (CO_2Me); δ_H 8.45 (1H, s, H-7), 7.66 (2H, s, H-4 and H-5), 7.50 (1H, d, H-3, *J* 5), 7.3 (1H, d, H-2, *J* 5), 6.87 (1H, s, =CH) and 3.9 (3H, s, OMe).

Methyl 2-azido-3-(7-methoxy-4-benzo[*b*]thienyl)propenoate 25

This compound was similarly obtained from 7-methoxybenzo-[*b*]thiophene-4-carbaldehyde as crystalline material (60%), mp 126–128 °C; ν_{max}/cm^{-1} 2120 (CN_3) and 1710 (CO_2Me); δ_H-($CDCl_3$) 8.17 (1H, d, H-5, *J* 10), 7.51 (1H, s, CH=), 7.43 (1H, d, H-6, *J* 10), 7.39 (1H, d, H-3, *J* 8), 6.73 (1H, d, H-2, *J* 8), 3.82 (3H, s, OMe) and 3.76 (3H, s, CO_2Me).

Methyl 8*H*-thieno[3,2-*g*]indole-7-carboxylate 26

A solution of **24** (70 mg, 0.27 mmol) in dry xylene (5 ml) was refluxed for 3 h. After cooling, the mixture was evaporated under reduced pressure and the crude product was purified by chromatography over silica gel (eluent, light petroleum–ethyl acetate, 9 : 1) to afford **26** as a white solid (30 mg, 50%), mp 185–187 °C (Found: C, 61.95; H, 4.18; N, 6.00. $C_{12}H_9O_2NS$ requires C, 62.33; H, 3.92; N, 6.05%); ν_{max}/cm^{-1} 3300 (NH) and 1690 (CO_2Me); δ_H 10.64 (1H, br s, NH), 7.68 (1H, d, H-4, *J* 8.7), 7.60 (1H, d, H-5, *J* 8.7), 7.46 (1H, d, H-3, *J* 5.4), 7.42 (1H, H-2, *J* 5.4), 7.35 (1H, d, H-6, *J* 2) and 4.04 (3H, s, CO_2Me); *m*/*z* (EI) 231 (M^+) and 171, 145.

Methyl 4-methoxy-6*H*-thieno[3,2-*e*]indole-7-carboxylate 27

This compound was similarly obtained from methyl 2-azido-3-(7-methoxy-4-benzo[*b*]thienyl)propenoate **25** as a crystalline material which was crystallised from ethanol, (81%), mp 225–226 °C; ν_{max}/cm^{-1} 3320 (NH) and 1690 (CO_2Me) (Found: C, 59.36; H, 4.43; N, 5.19. $C_{13}H_{11}O_3NS$ requires C, 59.77; H, 4.21; N, 5.36%); δ_H([$^2H_6$]DMSO, 200 MHz), 12.01 (1H, br s, NH), 7.79 (2H, s, H-1 and H-2), 7.50 (1H, d, *J* 2, H-8), 6.9 (1H, s, H-5), 3.97 (3H, s, OMe) and 3.85 (3H, s, CO_2Me); *m*/*z* (EI) 261 (M^+), 230 and 202.

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