Certain aspects of the chemistry of hydroxybenzo[b]thiophene[†]

CHANDRANI MUKHERJEE AND ASISH DE*
Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata
700 032, India.
email:ocad@mahendra.iacs.res.in, Phone:91-33-4734971; Fax:91-33-4732805.

Abstract

Hydroxybenzo[b]thiophene is an important benzo[b]thiophene derivative because of its role as an intermediate in the synthesis of condensed sulfur heterocycles. The hydroxyl group can be converted into *O*-carbamate and the latter utilized in the regiocontrolled introduction of substituents through directed metallation. In the present review, synthesis, properties and reactions of various hydroxybenzo[b]thiophenes are described.

Keywords: Hydroxybenzo[b]thiophene, thienobenzopyran, thienobenzopyranone, directed metallation.

1. Introduction

Benzo[b]thiophene, second in importance to thiophene among sulfur heterocycles and discovered soon after the latter's discovery, has attracted scant attention at that time, apart from some interest shown towards thioindigo dyes. The scenario has, however, changed with the advent of bioisosterism when organic chemists started showing interest in benzo[b]thiophene since it is a bioisoster of indole. Indeed, the main area of activity in the chemistry of benzo[b]thiophene, in the sixties and seventies of the last century, centred around the synthesis of its derivatives that are analogues of bioactive indole derivatives including indole alkaloids.The synthesis of several sulfur analogues of bioactive furanochromones and furanocoumarins are also reported in the literature. These analogues, consisting of a benzo[b]thiophene core, are usually obtained from the latter through suitable annulation reactions. This line of work continues till date and its literature up to 1980 has been reviewed.[1,2] In the present review, an account is given of the chemistry and uses of hydroxybenzo[b]thiophenes. The interest which this class of compounds has received, among the benzo[b]thiophene derivatives, is principally due to their usefulness in the (a) synthesis of sulfur analogues of several important bioactive indole derivatives, viz. serotonin, and (b) annulation of oxygenated rings onto the benzo[b]thiophene core.

Hydroxyl function has been incorporated at 2-, 3-, 4-, 5-, 6- and 7-positions in benzo[b]-thiophene, though not all the hydroxybenzo[b]thiophenes have received equal attention. Relatively easily accessible ones were better exploited. Among these, 2- and 3-hydroxybenzo[b]-thiophenes (**1** and **2**) exist principally as tautomers[1] and have been variously called as benzo[b]-thiophene-2(3H)-one, 2,3-dihydrobenzo[b]thiophene-2-one, thiooxindole, benzo[b]thiophene-3(2H)-one, 2,3-dihydrobenzo[b]thiophene-3-one and thioindoxyl.

[†] Dedicated to Prof. S. C. Bhattacharyya.
* Author for correspondence.

2. Spectroscopy

Spectroscopic studies on the parent benzo[*b*]thiophene and various substituted benzo[*b*]-thiophenes have been exhaustively reported in the literature. These studies, which include UV, IR, NMR and photo electron (PE) spectra, have thrown important light on the molecular structure of benzo[*b*]thiophene derivatives.

Thus, evidence for the existence of thiooxindole (**1**) and thioindoxyl (**2**) as tautomers in solution came from UV spectral studies. The UV spectrum of **1** closely resembles[3] that of the thiolactone (**3**). Similar conclusion about thioindoxyl (**2**) came from a comparison of its UV spectrum with that of the methyl ether of its enol.[4] The UV spectrum of **2** has been assigned[5] on the basis of molecules-in-molecules (MIM) calculation. Pariser-Parr-Pople method has been utilized[6] to calculate the electronic spectrum of the 2-benzylidene derivative of **2** and to find evidence[7] that it exists as tautomer. UV spectrum of 5-hydroxybenzo[*b*]thiophene-4,7-quinone was also recorded.[8] Spectroscopic measurements were utilized[9] to calculate the thermodynamic ionization constants of several hydroxybenzo[*b*]thiophenes.

Further evidence[10–13] of the existence of 2- and 3-hydroxybenzo[*b*]thiophenes came from their IR spectra, which also showed that when an adjacent carbonyl function is present, the enolic form predominates.[13–16] It was also shown[17] that 3-hydroxy-2-nitrobenzo[*b*]thiophene-1,1-dioxide exists as a mixture of keto and enol forms. Another application of spectroscopy[18,19] is in studying hydrogen bonding in several substituted 5-hydroxybenzo[*b*]thiophenes.

Detailed studies on ^{1}H[20,21] and ^{13}C[22,23] NMR spectra of variously substituted benzo[*b*]-thiophenes have been published which deal at length with the substituent effect on chemical shifts. Like UV and IR spectroscopy, NMR spectroscopy was also used to study[24–29] tautomerism of 3-hydroxybenzo[*b*]thiophene. It was shown[30] that 3-hydroxy-2-methyl- benzo[*b*]thiophene exists largely and the corresponding 2-phenyl derivatives exclusively as enol.

3. Preparation

Treatment of 2-benzo[*b*]thienyl lithium with oxygen affords thiooxindole (**1**)[31–33], which was also obtained from 2-aminobenzo[*b*]thiophene[31] through acid treatment on the diazonium salt derived from it or on itself. Alkali treatment of ethyl 2-acetamidobenzo[b]thiophene-3-carboxylate,[34] ethyl 2-aminobenzo[b]thiophene-3-carboxylate[34] or 3-bromobenzo[b]thiophene[35] results in the formation of thiooxindole (**1**). The last of the three reactions proceeds via the formation of 2,3-dehydrobenzo[*b*]thiophene and is accomplished by the formation of considerable amount of benzo[*b*]thiophene. Acid-mediated ring closure[36] of *ortho*-mercaptophenylacetic acid also affords (**1**).

Thioindoxyl (**2**) is obtained by ring closure of thiophenylacetic acid (**4**).[1] Base-induced ring opening[37,38] of 4-hydroxy-2-oxopyrano[3,2-*b*]benzo[*b*]thiophene (**5**) also affords thioindoxyl derivatives. There is an early report[39] on the synthesis of 4-hydroxybenzo[*b*]thiophene (**6**) from thiophene-2-carboxaldehyde (Scheme 1).

Both 4-[40] and 7-[41] hydroxybenzo[*b*]thiophenes (**6** and **7**) are obtained from the ketones **8** (R = H) and **9** (R = H). Dehydrogenation[42,43] of 6,7-dihydrobenzo[*b*]thiophene-4(5*H*)-one (R = H) with sulfur in hot diphenyl ether was practised earlier. We observed[40] that the two-step process[44]
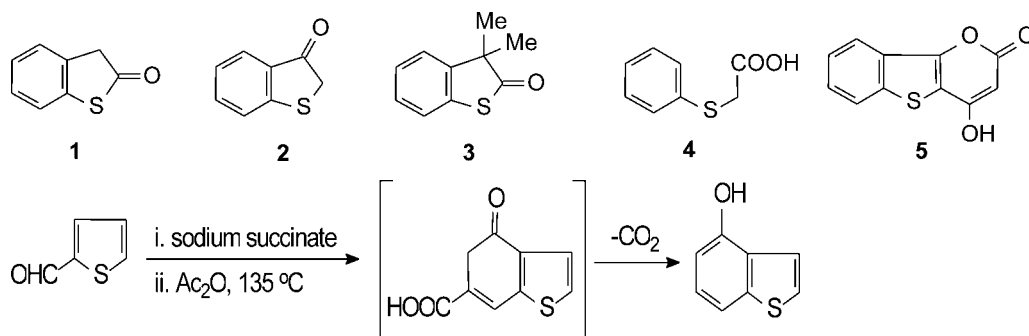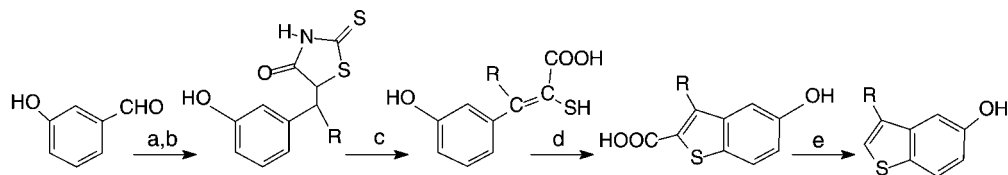
Scheme 1.

consisting of bromination of **8** (R = H) followed by dehydrobromination with LiBr and Li_2CO_3 in dry DMF affords a cleaner **6** in better overall yield. Consequently, we prepared **7** from **9** (R = H) in the same way.
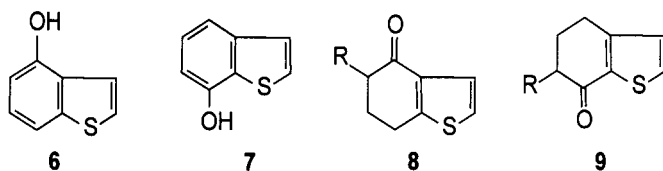
The widely applied general method of synthesis of benzo[*b*]thiophene, consisting of cyclization of intermediate mercaptoacrylic acid was utilized in the synthesis of 4-, 5-, 6- and 7-hydroxybenzo[*b*]thiophenes.[45–48] Synthesis of the last compound consists of conversion of 7-chloro to 7-hydroxy function.
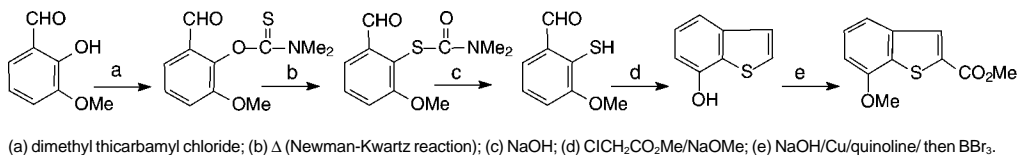
The process as shown in the synthesis of 5-hydroxybenzo[*b*]thiophene derivative (Scheme 2) consists of condensation of either a hydroxybenzaldehyde or the corresponding ketone with rhodamine followed by alkaline hydrolysis of the benzylidene rhodamine to afford the mercaptoacrylic acid. Cyclization of the latter, accomplished with iodine or chlorine, affords the hydroxybenzo[*b*]thiophene-2-carboxylic acid. Decarboxylation with copper-quinoline gives the desired hydroxybenzo[*b*]thiophene.

(a) rhodamine; (b) NaOMe; (c) NaOH; (d) I_2/1,4-dioxane and (e) Cu/quinoline/Δ.

Scheme 2.

Both 5- and 6-hydroxybenzo[*b*]thiophenes were prepared from the corresponding amino compounds via diazotization.[49,50] Fries rearrangement of 4-acetoxybenzo[*b*]thiophene affords 4-acetyl-5-hydroxybenzo[*b*]thiophene.[51] Similarly, Claisen rearrangement of 4-allyloxybenzo[*b*]thiophene gives 4-ally1-5-hydroxybenzo[*b*]thiophene.[52]

(a) dimethyl thicarbamyl chloride; (b) Δ (Newman-Kwartz reaction); (c) NaOH; (d) ClCH$_2$CO$_2$Me/NaOMe; (e) NaOH/Cu/quinoline/ then BBr$_3$.
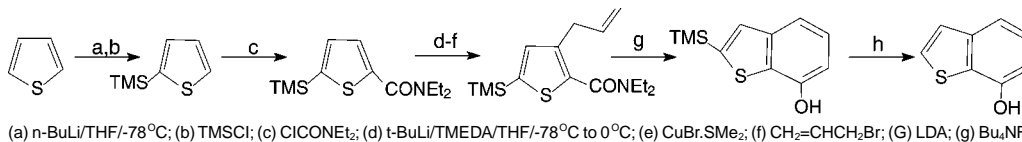
Scheme 3.

Synthesis of 7-hydroxybenzo[b]thiophene (7) was earlier accomplished through circuitous routes.[48, 53] The product obtained by demethylation of the corresponding methyl ether was said to be unstable. 7-Hydroxy-3-methylbenzo[b]thiophene was obtained[48] from 7-chloro compound via Grignard reagent through entrainment method.

The first practical synthesis of 7 through demethylation of the methyl ether was reported by Rahman and Scrowston[54] (Scheme 3) starting from o-vanilin. We have developed three expedient routes to 7. As stated above it was obtained through bromination–dehydrobromination of 5,6-dihydrobenzo[b]thiophene-7(4H)-one (9, R = H). Compound (9, R = H) was earlier obtained through lengthy and expensive routes. We devised a shorter route[40] to this compound from commercially available starting material (Scheme 4).

(a) I$_2$/Ph$_3$P/imidazole; (b) CH$_2$(COOEt)$_2$; (c) KOH; (d) Δ; (e) PPA
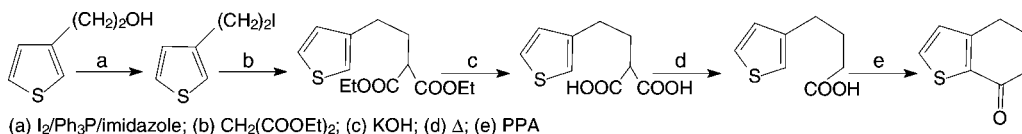
Scheme 4.

Two other routes[55] to 7 (Schemes 5 and 6) used 2-trimethylsilylbenzo[b]thiophene and 2-methoxycarbonylbenzo[b]thiophene, respectively. In the first of these, introduction of CONEt$_2$ function in the free α-position of 2-trimethylsilylbenzo[b]thiophene was followed by directed metallation in the position adjacent to the amide and then transmetallation–cyclization protocol. The third route to 7 (Scheme 6) involves base-catalyzed reaction of 2 methoxy-carbonylthiophene with γ-butyrolactone (Scheme 4) and the product upon alkaline hydrolysis afforded the keto alcohol, which was oxidized with PCC. The resulting keto aldehyde was cy-clized with boron trifluoride-methanol to afford 7-methoxybenzo[b]thiophene which was demethylated to give 7-hydroxybenzo[b]thiophene.

(a) n-BuLi/THF/-78°C; (b) TMSCI; (c) ClCONEt$_2$; (d) t-BuLi/TMEDA/THF/-78°C to 0°C; (e) CuBr.SMe$_2$; (f) CH$_2$=CHCH$_2$Br; (G) LDA; (g) Bu$_4$NF.

Scheme 5.

(a) γ-butyrolactone; (b) NaOMe; (c) 1,4-dioxane; (d) NaOH; (e) PCC; (f) BF$_3$-MeOH, MeOH, (g) BBr$_3$.
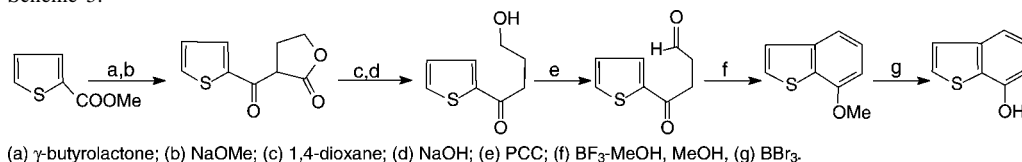
Scheme 6.

Flash vacuum pyrolysis of the condensation product (**10**) of 3-methylthiophene-2-carboxaldehyde and isopropylidinemalonate affords 5-hydroxybenzo[*b*]thiophene in 96% yield,[56] and 6-hydroxy-2-methylbenzo[*b*]thiophene was similarly obtained in near quantitative yield. Alkali-induced ring opening–ring closure of the pyrilium salt (**11**) results in the formation of 6-R-substituted-7-hydroxybenzo[*b*]thiophene.

Demethylation[57] of 5,6-dimethoxybenzo[*b*]thiophene-2-carboxylic acid, obtained by cyclizing[57, 58] intermediate mercaptoacrylic acid affords 5,6-dihydroxybenzo[*b*]thiophene. Catalytic reduction[59] of benzo[*b*]thiophene-4,7-quinone gives 4,7-dihydroxybenzo[*b*]thiophene, which is unstable.

4. Reactions

Thiooxindole (**1**) reacts with diazomethane to give a spirooxadiazole.[59] Formylation of (**1**) in the 3 position is accomplished by alkaline hydrolysis[60] of the anil formed by condensation with diphenylformamidine and of the condensation product between indoxy1 and benzo[*b*]thiophene-2,3 quinone by Gatterman reaction.[61] The yield of the last reaction is mediocre. Thiooxindole (**1**) undergoes base-catalyzed condensation with the formyl derivatives. Fusion of (**1**) and *N,N*-diphenylacetamide affords an anil which can be hydrolyzed to 3-acetyl thiooxindole.[62] Thioindoxyl (**2**) and substituted thioindoxyl undergo formylation in the 2-position by Gattermann reaction.[61] Vilsmeier reaction on thioindoxyl affords 3-chlorobenzo[*b*]thiophene-2-carboxaldehyde. Thioindoxyl and substitued thioindoxyls are reduced to the coressponding benzo[*b*]thiophene with zinc or tin and acid[63] or with sodium borohydride.[64] Reduction by Wolff–Kishner[65,66] or Clemmensen[67] methods afford 2,3-dihydrobenzo[*b*]thiophene. Thioindoxyl undergoes Reformatsky reaction with ethyl bromoacetate.[68] The reactive methylene group in the 2-position of thioindoxyl undergoes various condensation reactions, viz. with aromatic aldehydes[69–72] or with *p*-nitro-*N,N*-dimethylaniline. In the presence of sodium methoxide, 2-(aryl)thioindoxyls are alkyaled in the 2-postion and also undergo *O*-alkylation.[73]

Among the hydroxybenzo[*b*]thiophenes with hydroxyl groups in the benzene ring, 4- and 5-hydroxybenzo[*b*]thiophenes are used in the preparation of sulfur analogues of bioactive naturally occuring indoles like psilocin[74] or serotonin,[75] through incorporation of side chain in the thiophene ring. These hydroxybenzo[*b*]thiophenes undergo smooth *O*-alkylation with alky1 hailde. *O*-sulfonylation[76] has been reported for 5-hydroxy benzo[*b*]thiophene which also reacts[77] with epichlorohydrin to afford 5-(3-chloro-2-hydroxypropoxy)benzo[*b*]thiophene. *O*-carbamates derived from those hyroxybenzo[*b*]thiophenes are used as pesticides, viz. mobam (**12**) which has low mammalian toxicity. *O*-carbamates derived from 4- and 5-hydroxybenzo[*b*]thiophenes are useful in the regiocontrolled introduction of functionalities in the benzene rings (see later). Alkylation of 4- and 5-hydroxybenzo[*b*]thiophenes with chloromethyl methyl ether affords 4- and 5-OMOM derivatives which serve as donors in electron transfer reactions.[78] We have reported[40] an interesting and somewhat unusual reaction of the phenoxide anion derived from 4-hydroxybenzo-[*b*]thiophene with γ-butyrolactone (Scheme 6) leading to alkyl oxygen ring fission of the latter affording (**13**). This compound is a synthetic intermediate in the annulation of a seven-membered oxygen ring on to the benzo[*b*]thiophene core. Epichorohydrin reacts[78] with 4-hydroxybenzo-[*b*]thiophene in the same way it does with indoxyl.
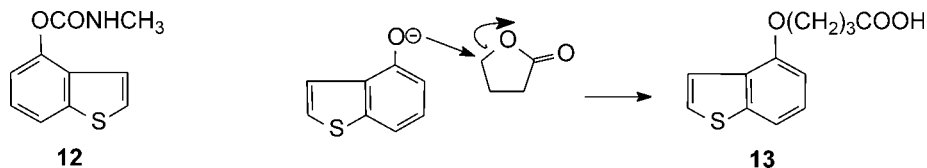
Electrophilic substitution reactions on those hydroxybenzo[*b*]thiophenes often give mono and disubstituted derivatives. Thus, 4-hydroxybenzo[*b*]thiophenes[79,80] upon bromination with molecular bromine and nitration gives 5,7-disubstituted products. Bromination of 5-hydroxybenzo-[*b*]thiophene gives 4,6-dibromoderivatives.[81] Nitration of 5-hydroxybenzo[*b*]thiophenes with cold nitric acid gives 4-nitro derivative. Bromination and nitration of 6-hydroxybenzo[*b*]thiophene gives 7-bromo as well as 2,7-dibromo derivatives and both 5-nitro and 2-nitro derivative.[82] 7-Hydroxy-3-methylbenzo[*b*]thiophene[48] gives 6-bromo derivative upon bromination with molecular bromine and 4-bromo derivative with *N*-bromosuccinimide. Nitration of this compound affords 6-nitro and 4,6-dinitro derivatives along with 4,7-quinone. Both 4- and 5-hydroxybenzo-[*b*]thiophene undergo modified Gattermann reaction[1] using anhydrous zinc cyanide and HCl gas leading to formylation in 5 and 4 postions, respectively.

5. Use of hydroxybenzo[*b*]thiophenes in directed metallation

Heteroatom-directed *ortho*-metallation, popularly termed directed metallation is recognized as a versatile weapon in the armamentarium of organic chemist and is particularly useful in regiocontrolled introduction of functional groups in aromatic and heteroaromatic molecules.[83] Surprisingly, this methodology remained practically unsused for a long time in benzo[*b*]thiophene chemistry. The use of standard directed metallation–transmetallation–allylation–cyclization protocol leading to an expedient synthesis of 7-hydroxybenzo[*b*]thiophene is described above. Reported below is an account of our endeavor of regiocontrolled introduction of functionalities in benzo[*b*]thiophene molecule using directed metallating groups (DMG) derived from hydroxyl functions in hydroxybenzo[*b*]thiophenes.

We used methoxy and *O*-carbamate functions as DMGs, easily obtained via *O*-alkylation of the hydroxyl groups in 4-, 5- and 7-hydroxybenzo[*b*]thiophenes. Regiocontrolled functionalization of the benzene ring in benzo[*b*]thiophene is difficult because of the greater reactivity of the α-position in thiophene ring. Introduction of a suitable functionality *ortho* to the DMG is important to obtain intermediates that can be used for annulating a third ring on to the benzo[*b*]thiophene core. Of the two DMGs, *O*-carbamate has more powerful directing power.[83]

Under standard directed metallating condition,[83] (*sec*-BuLi or *t*-BuLi/TMEDA/THF/–78°C) benzo[*b*]thiophene with methoxy or *O*-carbamyl functions in 4-, 5-, 6-, or -7 positions are deprotonated exclusively in the 2-position.[84–86] When this position is suitably protected, deprotonation occurs under identical conditions, *ortho* to the DMG. It is surmised (see later) that deprotonation α to the ring sulfur atom is kinetically controlled while directed metallation *ortho* to the DMGs in benzo[*b*]thiophene is controlled thermodynamically. The *ortho* deprotonated molecules have been quenched with representative electrophiles like methyl iodide, *N, N*-dimethyl formamide and tributyltin chloride. Not unexpectedly, directed metallation of methoxy compounds was comparatively sluggish. It is interesting to note that 5-*O*-carbamate deprotonates

exclusively in the 4-postion[86] and the deprotonated species can be quenched with electrophiles leading to 4-substituted products. This is in contrast to the normal electrophilic subsitution undergone by 5-hydroxybenzo[b]thiophene in which both positions *ortho* to the hydroxyl group are attacked leading to disubstitution (see above).

An *ortho*-lithio derivative obtained by directed metallation of an *O*-carbamate undergoes intramolecular anionic Fries rearraangement[87] affording salicyl amide, if the lithiated species is not reacted with an electrophile. Such rearrangement has been carried out[84,85] on 4-, 5- and 7-hydroxybenzo[b]thiophenes. No protection of the α-position to the ring sulfur atom was necessary during these rearrangements. It is therefore surmised that when *O*-carbamates derived from the hydroxybenzo[b]thiophene are subjected to directed metallation, deprotonation presumably occurs both at the positions α to the ring sulfur atom and *ortho* to the DMG. While the kinetic acidity of the protons α to the ring sulfur atoms leads to substituted products upon electrophile quenching, in the absence of an electrophile, the thermodynamically controlled species, *ortho* to the DMG, predominate. More experiments are needed to verify this conjecture.

Salicyl amides obtained via anionic Fries rearrangement are useful synthetic intermediates since a fresh DMG, viz. CONEt$_2$ is generated during the course of this rearrangement. We have utilized[84,87,88] this phenomenon for annulating 6-membered oxygenated rings on to the existing benzo[b]thiophene core (Scheme 7).
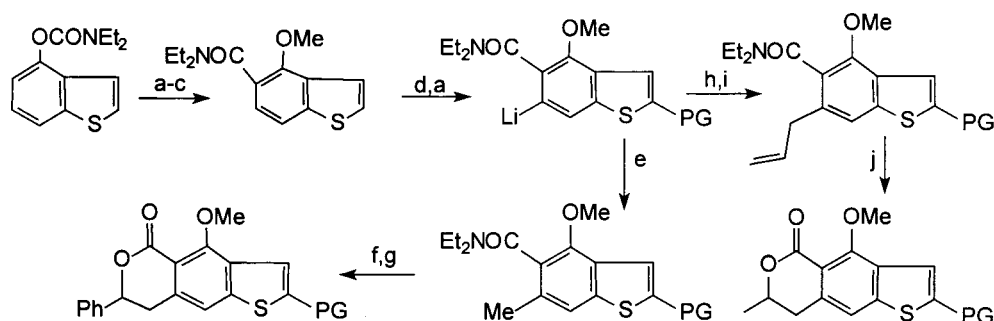
(a) *s*-BuLi/TMEDA/THF/-78°C; (b) -78°C-RT, 12 h; (c) MeI/K$_2$CO$_3$; (d) *n*-BuLi/TBDMSCl; (e) MeI; (f) LDA/PhCHO; (g) NaOH; (h) CuBr.SMe$_2$;; (i) CH$_2$=CHCH$_2$Br; (i) HCl.

Scheme 7.

6. Hydroxybenzo[b]thiophenes in annulation reactions

Hydroxybenzo[b]thiophenes are used as intermediates in reactions for annulating an oxygenated ring on to the benzo[b]thiophene core either on the benzene or on the thiophene ring. Annulations can be carried out either through introduction of a suitable functionality *ortho* to the hydroxyl group, followed by reaction with an annulating agent or by *O*-allylation-[3,3]sigmatropic rearrangement–cyclization protocol.

Synthesis of compounds formed by annulation of a 5- or 6-mermbered oxygen heterocycle either linearly or angularly to the benzene ring of benzo[b]thiophene began for making sulfur analogues for bioactive furanochromones or furanocoumarins. This expectation is pertinent in
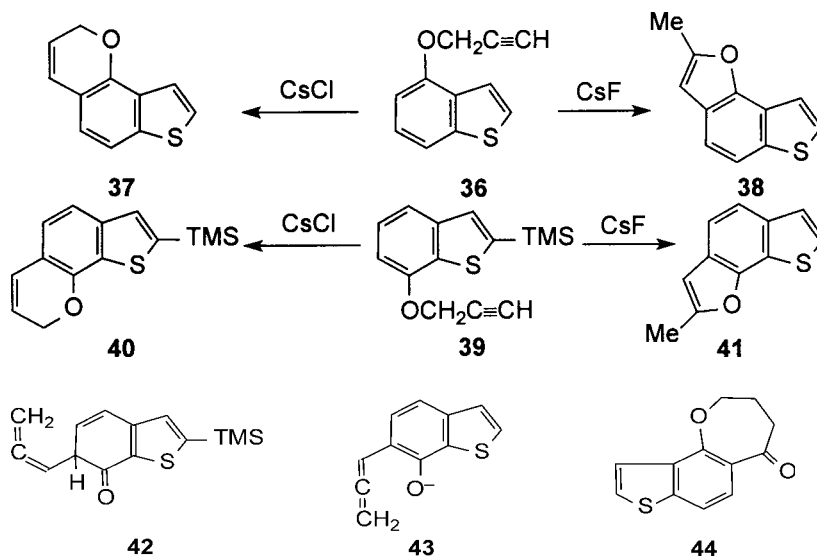
view of the marked higher biological activity shown by sulfur analogues of biologically inactive tricyclic compounds consisting of benzo[*b*]furans with condensed isoxazole, thiazole or pyrazole moities. The furocoumarins and furochromones, which inspired the synthesis of their sulfur analogues, are naturally occurring compounds, showing pronounced biological activities. Synthesis of sulfur analogues of furochromones and furocoumarins from hydroxybenzo[*b*]thiophenes was first reported by Mustafa *et al.*[51] who synthesized 2-methylthieno[3,2-*f*][l]benzopyran-4-one (**14**) and thieno[3,2-*f*][l]benzopyran-2-one (**15**).

Chapman and coworkers[89] used von Pechman reaction to synthesize thienocoumarins which consist of reaction of the corresponding hydroxybenzo[*b*]thiophene with ethylaceto acetate. Compounds **16–19** were thus synthesized from 5-hydroxybenzo[*b*]thiophene,[90] 4-hydroxybenzo-[*b*]thiophene,[90a] and 4-hydroxy-3-methylbenzo[*b*]thiophene[90a] and 7-hydroxy-3 methylbenzo[*b*]-thiophenes,[91] respectively. A number of thieno[2,3-*h*][l]benzopyranones (**20**) and thieno[3,2-*f*][l]-benzopyranones (**21**) were synthesized by De and coworkers[92] from 4- and 5-hydroxy benzo[*b*]-thiophenes carrying an aldehyde function *ortho* to the hydroxyl group. A detailed NMR study[93] was also carried out on these compounds.

Among the tricyclic compounds consisting of furan ring fused to benzo[*b*]thiophene, ethyl thieno[3,2-*e*][l]benzo[*b*]thiophene-2-carboxylate (**22**) and ethyl thieno[2,3-*g*][1]benzo[*b*]thiophe-necarboxylate (**23**)[51] were obtained by the reaction of 4-hydroxybenzo[*b*]thiophene-5-carboxaldehyde and 5-hydroxybenzo[*b*]thiophene-4-carboxaldehyde with diethyl bromomalonate. De and coworkers prepared[94] **24** and **25** by reacting 4-hydroxybenzo[*b*]thiophene-5-carboxaldehyde with *p*-nitrophenacyl bromide.

Reports on tricyclic compounds obtained by annulation of oxygenated rings to the thiophene ring of benzo[*b*]thiophene are fewer in number. Chatterjea and Sahai[95] synthesized 1*H*[1]benzothieno[3,2-*c*]pyran and 1*H*[1]-benzothieno[2,3-*c*]pyran (**26**) systems from dimethyl benzo[*b*]thiophene-2,3-dicarboxylate. There is a report[96] on the synthesis of 4-phenyl-2*H*[1]benzothieno[3,2-*b*]pyran-2-one (**27**) from thiosalicylic acid and 3-phenylpent-2-enedioic acid. Elegant use of [1]benzothieno[2,3-*c*]pyran-3-one and [1]benzothieno[3,2-*c*] pyran-3-one by Jackson and Moody[97] in cycloaddition reactions through *in situ* thermal generation of quino-dimethane and use of [1]benzothieno[3,2-*b*]pyran as an additive in fuel oil[98] and of [1]benzothieno-[3,2-*b*]furan as antidepressent[99] have been reported.

Annulation of a 6-membered oxygen heterocycle through [3,3] sigmatropic rearrangement–cyclization protocol on to the benzene ring of benzo[*b*]thiophene has been investigated in our laboratory.[52] Reaction of 4-hydroxy and 5-hydroxybenzo[*b*]thiophene with 3-chloro-3-methylbut-l-yne in the presence of anhydrous potassium carbonate and heating of the resulting ether underwent sequential Claisen rearrangement and cyclization to afford **28** and **29**. Interesting observations were made[52, 85] during the annulation reactions through the alkylation of the hydroxyl function with allyl and propargyl bromide followed by rearrangement and ring closure. Both 4-allyloxy (**30**) and 7-allyloxybenzo[*b*]thiophene (**33**) underwent smooth thermal rearrangement and the rearranged products afforded 2-methyl-2,3-dihydrothieno[3,2-*g*][1]benzofuran (**32**) and 2-methyl-2,3-dihydrothieno[2,3-*g*][1]benzofuran (**35**), respectively, through PPA-mediated cyclization (Scheme 8).

14   15   16   17, R = H   19
           18, R = Me

20   21   22   23, R = Me, R = COOEt
R = CN, COOEt, CONH₂   24, R = H ; R' = 4-nitrophenyl
R' = H, Me, Br   25. R = Me; R' = 4-nitrophenyl

26   27   28   29

30   31   32

33   34   35

Scheme 8.

Propargyloxybenzo[b]thiophenes (**36** and **39**) underwent one-pot thermal rearrangement–ring closure. The ring closure step could be modulated by proper choice of additive.[85] Annulation of 6-membered rings resulted from the rearrangement in the absence of additives or in the presence of CsCl. Use of CsF however resulted in the annulation of 5-membered ring (Scheme 9).

The role of additives in the Claisen rearrangement of primary ethers was earlier highlighted by Japanese chemists.[100] The α-allenylketone (**42**) formed during the sigmatropic rearrangement undergoes enolization followed by hydrogen shifts and ring closure. CsCl apparently facilitates this process. CsF, on the other hand, abstracts the α-hydrogen atom from the allenylketone to afford **43** which then undergoes ring closure.

Scheme 9.

We have reported the opening of γ-butyrolactone ring with the anion derived from 4-hydroxy-benzo[*b*]thiophene leading to the oxoacid (**13**). PPA-induced cyclization of the latter results in tricylic system (**44**) consisting of a 7-membered oxygenated ring fused to the benzene ring of benzo[*b*]thiophene.[101]

Acknowledgement

References

1. IDDON, B. AND SCROWSTON, R. M.   *Advances in heterocyclic chemistry,* Vol. 11 (A. R. Katritzky, ed.) Academic Press, 1970, p.177.

2. SCROWSTON, R. M.   *Advances in heterocyclic chemistry,* Vol. 29 (A. R. Katritzky, ed.) Academic Press, 1981, p.171.

3. STACY, G. W. AND WOLLNER, T. E.   *J. Org. Chem.,* 1967, **32**, 3028.

4. OKSENGENDLER, G. M. AND MOSTOSLAVSKII, M. A.   *Ukr. Khim. Zh.* 1960, **26**, 69; *Chem. Abstr.,* 1960, **54**, 14934.

5. KRESZE, G. AND AMANN, W.   *Spectrochim. Acta A,* 1968, **24**, 1283.

6. MOSTOSLAVSKII, M. A. AND YUGAI, G. A.   *Ukr. Khim. Zh. Russ. Edn,* 1976, **42**, 1219; *Chem. Abstr.,* 1977, **86**, 105253.

7. MINKIN, V. I., KOSOBUTSKII, V. A. SIMKIN, B. YA. AND ZHDANOV, YU. A.   *J. Mol. Struct.,* 1975, **24**, 237.

8. SPRUIT, C. J. P. *Rec. Trav. Chim.,* 1962, **81**, 810.

9. DEMERSEN, P. *et al.* *Bull. Soc. Chim. Fr.,* 1965, 1464.

10. STACY, G. W., VILLAESCUSA, F. W. AND WOLLNER, T. E. *J. Org. Chem.,* 1965, **30**, 4074.

11. STACY, G. W. AND WOLLNER, T. E. *J. Chem. Soc.,* 1967, **32**, 3028.

12. HOLT, S. J. KELLIE, A. E., O'SULLIVAN, D. G. AND SADLER, P. W. *J. Chem. Soc.* 1958, 1217.

13. MULHOLLAND, T. P. C., HONEYWOOD, R. I. W., PRESTON, H. D. AND ROSEVEAR, D. T. *J. Chem. Soc.,* 1965, 4939.

14. BROOKE, G. M. AND QUASEM, M. A. *J. Chem. Soc. C,* 1967, 865.

15. JAKOBSEN, H. J. AND LAWESSON, S. O. *Tetrahedron,* 1965, **21**, 3331.

16. HEINDEL, N. D., FISH, V. B. RYAN. M. F., AND LEPLY, A. R. *J. Org. Chem.,* 1967, **32**, 2678.

17. MATSKANOVA, M. A. AND ARENS, A. *Latvijas PSR Zinatnee Akad. Vestis, Kim. Ser.,* 1966, 362, *Chem. Abstr.*, 1966, **65**, 15193.

18. BROWN, L., EGLINTON, G. AND MARTIN-SMITH, M. *J. Chem. Soc.,* 1963, 2551.

19. BROWN, L., EGLINTON, G. AND MARTIN-SMITH, M. *Spectrochim. Acta,* 1962, **18**, 1593.

20. CADDY, B., MARTIN-SMITH, M., NORRIS, R. K., REID, S. T. AND STERNHELL, S. *Aust. J. Chem.,* 1968, **21**, 1853.

21. CHAPMAN, N. B., EWING, D. F., SCROWSTON, R. M. AND WESTWOOD, R. *J. Chem. Soc. C,* 1968, 764.

22. PLATZER, N., BASSELTER, J. J. AND DEMERSEMAN, P. *Bull. Soc. Chim. Fr.,* 1974, 905.

23. CLARK, P. D., EWING, D. F. AND SCROWSTON, R. M. *Org. Magn. Reson.,* 1976, **8**, 252.

24. BROOKE, G. M. AND QUASIM, M. A. *J. Chem. Soc. C,* 1967, 865.

25. BUU-HOI, N. P., BELLAVITA, V. RICCI, A. AND GRANDOLINI, G. *Bull. Soc. Chim. Fr.,* 1965, 2658.

26. JAKOBSEN, H. J. AND LAWESSON, S. O. *Tetrahedron,* 1965, **21**, 3331.

27. EL SHANTA, M. S., SCROWSTON, R. M. AND TWIGG, M. V. *J. Chem. Soc. C,* 1967, 2364.

28. HUKE, M. AND GORLITZER, K. *Arch. Pharm.* (Weinheim Ger), 1969, **302**, 423.

29. CHAUHAN, M. S. AND STILL, I. W. J. *Can. J. Chem.,* 1975, **53**, 2880.

30. STRIDSBERG, B. AND ALLENMARK, S. *Chem. Scr.*, 1976, **9**, 216.

31.   VAN ZYL, G., DE JONGH, D. C.,   *J. Org. Chem.,* 1961, **26**, 4946.
      HEASLEY, V. L. AND VAN DYKE, J. W.

32.   VANZYL, G. *et al.*   *4th A. Rep. Petrol. Res. Fund,* Am. Chem. Soc., 1959, 39.

33.   VAN ZYL, G., DE JONGH, D. C.,   *J. Org. Chem.,* 1961, **26**, 4946.
      HEASLEY, V. L. AND VAN DYKE, J. W.

34.   GEWALD, K., NEUMAN, G. AND   *Z. Chem.,* 1966, **6**, 261.
      BOTTCHER, H.

35.   KOMPPAR, G. AND WECKMAN, S.   *J. Prakt. Chem.,* 1933, **138**, 109.

36.   IDDON, B. AND SCROWSTON, R. M.   *Advances in heterocyclic chemistry* (R. Katritzky, ed.), Academic
                                            Press, 1970, Vol. 11, p. 296.

37.   MUSTAFA, A. AND ISLAM, A. M.   *J. Chem. Soc.,* 1951, 1616.

38.   WYNBERG, H. AND CABELL, M.   *J. Org. Chem,* 1973, **38**, 2814.

39.   BEIDERMAN, A.   *Chem. Ber.,* 1886, **19**, 1605.

40.   MUKHERJEE, S., JASH, S. S. AND DE, A. *J. Chem Res.* (S), 1993, 192.

41.   SAMANTA, S. S., GHOSH, S. C.   *J. Chem. Soc, Perkin Trans.1,* 1997, 3673.
      AND DE, A.

42.   FIESER, L. F. AND KENNELLY, R. G.   *J. Am. Chem. Soc.,* 1935, **57**, 1611.

43.   NAPIER, R. P., *et al.*   *J. Heterocycl. Chem.,* 1970, **7**, 393.

44.   KASTURI, T. R. AND ARUNACHALAM, T.   *Can. J. Chem.,* 1968, **46**, 3625.

45.   CLARKE, K., SCROWSTON, R. M. AND   *J. Chem. Soc., Perkin Trans.1,* 1973, 1196.
      SUTTON, T. M.

46.   CHAKRABORTI, P. M., CHAPMAN, N. B.   *Tetrahedron,* 1969, **25**, 2781.
      AND CLARKE, K.

47.   CAMPAIGNE, E. AND KREIGHBAUM, W. E.   *J. Org. Chem.,* 1961, **26**, 1326.

48.   CHAPMAN, N. B., CLARKE, K. AND   *J. Chem. Soc., Perkin Trans. 1,* 1972, 1404.
      MANOLIS, A.

49.   BORDWELL, F. G. AND STANGE, H.   *J. Chem. Soc.,* 1955, **77**, 5939.

50.   HANSCH, C. AND SCHMIDHALTER, B.   *J. Org. Chem.,* 1955, **20**,1056.

51.   MUSTAFA, A., ZAYED, S. M. A. D.   *Ann. Chem.,* 1967, **704**, 176.
      AND EMRAN, A.

52.   DE, A., BRUNSKILL, J. S. A. AND   *Indian J. Chem. B,* 1984, **23**, 918.
      JEFFREY, H.

53.   SUNTHANKAR A. V. AND. TILAK, B. D.   *Proc. Indian Acad. Sci. A,* 1951, **33**, 35.

54.   RAHAMAN, L. K. A. AND   *J. Chem. Soc., Perkin Trans. 1,* 1983, 2972.
      SCROWSTON, R. M.

55.   SAMANTA, S. S., GHOSH, S. C.   *J. Chem. Soc., Perkin Trans. 1,* 1997, 2683.
      AND DE, A.

56. BAXTER, G. J., BROWN, R. F. C. AND   *Aust. J. Chem.,* 1974, **27**, 2605.
    McMULLEN, G. L.

57. BEW, D. G. AND CLEMO, G. R.   *J. Chem. Soc.,* 1953, 1314.

58. CAMPAIGNE, E. AND CLINE, R. E.   *J. Org. Chem.,* 1956, **21**, 39.

59. HAWTHORNE, D. G. AND PORTER, Q. N. *Aust. J. Chem.,* 1966, **19**, 1751.

60. GLAUERT, R. H. AND MANN, F. G.   *J. Chem. Soc.,* 1952, 2127; *British Patent*, 1952, **684**, 187; *Chem. Abstr.,* 1953, **47**, 6290.

61. TRUCE, W. E.   *Org. React.,* 1957, **9**, 37.

62. KIRSCH, G.   Personal Communication.

63. MUSTAFA, A. AND ZAYED, S. M. A. D. *J. Am. Chem. Soc.,* 1956, **78**, 6174.

64. CAMPAIGNE, E. AND KREIGHBAUM, W. E. *J. Org. Chem.,* 1961, **26**, 363.

65. PETROPOULOS, J. C., MCCALL, M. A.   *J. Am. Chem. Soc.,* 1953, **75**, 1130.
    AND TARBELL, D. S.

66. CARRUTHERS, W., DOUGLAS, A. G.   *J. Chem. Soc.,* 1962, 704.
    AND HILL, J.

67. MUTH, B. R. AND KISS, A. I.   *J. Org. Chem.,* 1956, **21**, 576.

68. MARTIN-SMITH, M. AND RAID, S. T.   *J. Chem. Soc. C,* 1967, 1897.

69. KUCHARCZYK, N. AND HORAK, V.   *Colln Czech. Chem. Commun.,* 1968, **33**, 92.

70. PEROLD, G. W. AND VAN LIGEN, P. F. A. *Chem. Ber.,* 1959, **92**, 293.

71. GUHA, S. K., CHATTERJEA, J. N.   *Chem. Ber.,* 1961, **94**, 3297.
    AND MITRA, A. K.

72. KUCHARCZYK, N. AND HORAK, V.   *Chem. Ind.* (Lond.), 1964, 976.

73.   *Netherlands Patent*, Appl. 6, 1965, **413**, 199; *Chem. Abstr.,* 1965, **63**, 18038. (E. Merck, A. G.)

74. CHAPMAN, N. B., SCROWSTON, R. M.   *J. Chem. Soc., Perkin Trans. 1,* 1972, 3011.
    AND SUTTON, T. M.

75. CHAPMAN, N. B. *et al.*   *J. Chem. Soc., Perkin Trans. 1*, 1973, 750.

76. MARTIN-SMITH, M., SNEADER, W. E.,   *J. Chem. Soc. C,* 1967, 1899.
    BROWN, I. AND REID, S. T.

77. TURNER, R. W.   *British Patent*, 1967, 089, 769, Imperial Chemical Industries Ltd, *Netherlands Patent, Appl.,* 6, 1967, 608, 718, *Chem. Abstr.*, 1968, **68**, 29586.

78. DE, A., KAMILA, S. AND MUKHERJEE, C. Unpublished work.

79. CAMPAIGNE, E., DINNER, A. AND   *J. Heterocycl. Chem.,* 1971, **8**, 755.
    HASEMAN, M.

80. CLARKE, K., SCROWSTON, R. M.   *J. Chem. Soc., Perkin Trans.1,* 1973, 1196.
     AND SUTTON, T. M.

81. BORDWELL, F. G. AND STANGE, H.   *J. Am. Chem. Soc.,* 1955, **77**, 5939.

82. CLARK, P. D., CLARKE, K.,   *J. Chem. Res (S)*, 1978, **10(N)**, 368.
     SCROWSTON, R. M. AND SUTTON, T. M.

83. SNIECKUS, V.   *Chem. Rev.,* 1990, **90**, 879.

84. MONDAL, S. S., SAMANTA, S. S.,   *J. Chem. Soc., Perkin Trans.1*, 1988, 2559.
     DEB, C. AND DE, A.

85. GHOSH, S. C. AND DE, A.   *J. Chem. Soc., Perkin Trans.1,* 1999, 3705.

86. MUKHERJEE, C.   Unpublished work.

87. SIBI, M. P. AND SNIECKUS, V.   *J. Org. Chem.,* 1983, **48**, 1835.

88. KAMILA, S. AND DE, A.   Unpublished work.

89. SETHNA, S. AND PHADKE, R.   *Org. React.,* 1953, **7**, 1.

90. a. CHAKRABORTI, P. M.   *J. Chem. Soc.,* 1970, 1.
     CHAPMAN, N. B. AND CLARKE, K.

     b. CLARKE, K., SCROWSTON, R. M.   *J. Chem. Soc., Perkin Trans.1,* 1973, 1196.
     AND SUTTON, T. M.

91. CHAPMAN, N. B., CLARKE, K. AND   *J. Chem. Soc., Perkin Trans.1,* 1972, 2593.
     MANOLIS, A.

92. ASPROU, C. M., BRUNSKILL, J. S. A.,   *J. Heterocycl. Chem.,* 1980, **17**, 87.
     JEFFREY, H. AND DE, A.

93. BROWN, N. M. D., DE, A., BRUNSKILL,   *Org. Magn. Reson.,* 1982, **18**, 11.
     J.S.A. AND JEFFREY, H.

94. DE, A. BRUNSKILL, J. S. A. AND   *Indian J. Chem. B,* 1984, **23**, 918.
     JEFFREY, H.

95. CHETTERJEA, J. N. AND SAHAI, R. P.   *J. Indian Chem. Soc.,* 1989, **59**, 1372.

96. BUGGLE, K., GHOGIN, V. N.   *J. Chem. Soc., Perkin Trans.1,* 1983, 1427.
     NANGLE, M. AND MACMANAS, P.

97. JACKSON, M. P. AND MOODY, C. J.   *J. Chem. Soc., Perkin Trans.1*, 1990, 681.

98. SELUCKY, M. L., WASEL, R.,   *Fuel Process. Technol.,* 1990, **26**, 117.
     RAWLUK, M., REBUS, B. AND
     TAERUM, T.

99. SASAKI, K., TASIMA, Y. AND HIROTA, T. *J. Heterocycl. Chem.,* 1991, **28**, 269.

100. ISHII, H. *et al.*   *Chem. Pharm. Bull.,* 1990, **38**, 1975.

101. MUKHERJEE, S. AND DE, A.   *J. Chem. Res.,* 1994, 295(S), 1735(M).