REACTION OF BENZO[b]THIOPHENE-5- AND 6-METHANOLS WITH n-BUTYLLITHIUM. DIRECTED LITHIATION IN THE BENZENE RING

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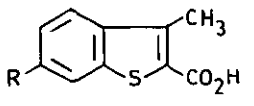
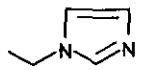
Abstract - The preparation of 3-methylbenzo[b]thiophene-6-methanol (3) is described. Treatment of 3 with n-butyllithium followed by CO_2 gave, in addition to the expected 2-carboxylic acid 2, a substantial quantity of the lactone 11 formed via lithiation at the 7-position. It was concluded that lithiation at the 7-position is favoured by a co-operative effect of the anion of the alcohol and the ring sulphur atom, as well as the 3-methyl group which reduces the rate of lithiation at the 2-position. In the case of compounds in which the alcohol group is at the 5-position or which lack the 3-methyl group, lithiation in the benzene ring was much less favoured.

In connection with the synthesis of some imidazolylmethylbenzo[b]thiophene thromboxane synthetase inhibitors, [1] several hydroxymethylbenzo[b]thiophene-2-carboxylic acids were required as intermediates. A particular target was 1 for which the hydroxymethyl intermediate 2 was needed.

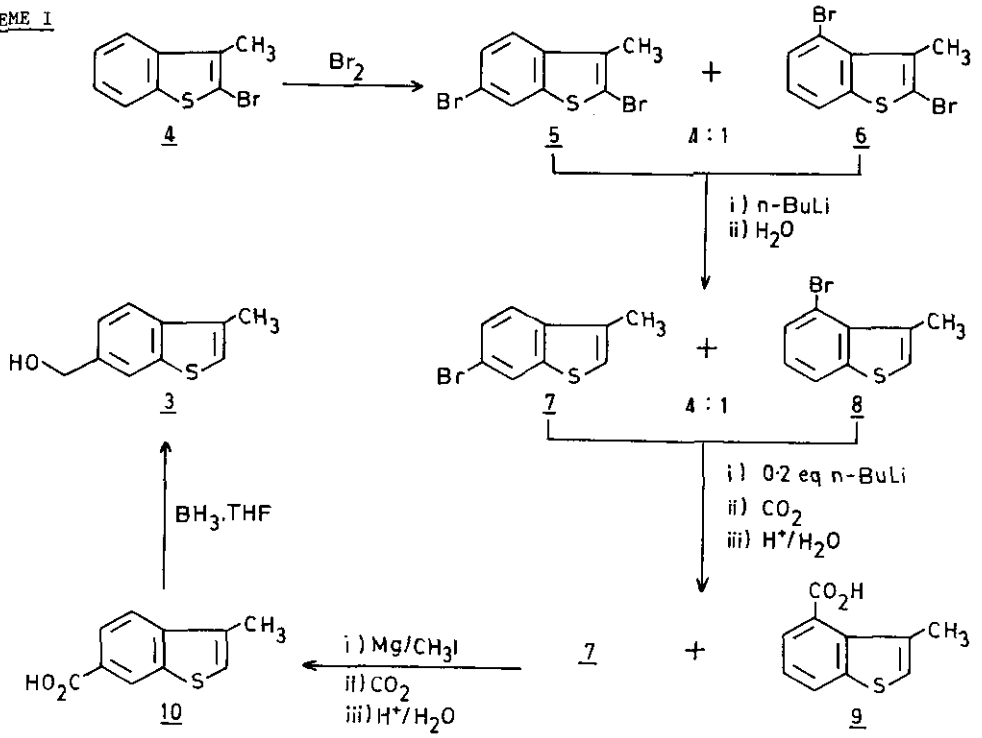


1, R= 

2, R=CH_2OH

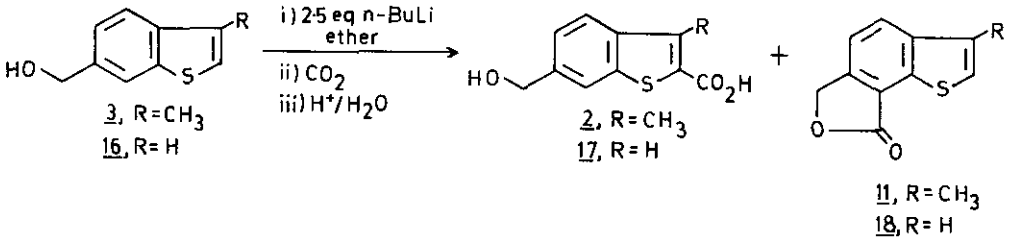
Benzo[b]thiophene-2-carboxylic acids are conveniently prepared by treatment of a benzo[b]thiophene with n-BuLi followed by CO_2.[2,3] Such an approach for the synthesis of 2 required the preparation of the alcohol 3 (Scheme I). 6-Bromo-3-methylbenzo[b]thiophene 7 was considered to be a suitable precursor to 3 since bromination of 2-bromo-3-methylbenzo[b]thiophene (4) is reported [4] to give exclusively the 2,6-dibromo compound 5 from which 7 should be available by selective mono-debromination. However, in our hands, bromination of 4 gave an inseparable mixture of 5 and what was shown by subsequent reactions to be the 2,4-dibromo isomer 6 in the ratio 4 : 1 (Scheme I). Treatment of the mixture with 1 equivalent of n-BuLi followed by hydrolysis gave a mixture of the monobromo isomers 7 and 8. It was found fortuitously that 8 reacted more rapidly with n-BuLi

SCHEME I



than 7 which provided a means of obtaining pure 7. Treatment of the mixture with just sufficient n-BuLi to react with the 8 present followed by CO_2 gave the acid 9, while distillation of the neutral fraction yielded pure 7. The greater reactivity of 8 than 7 may be ascribed to release of steric strain caused by peri - interaction of the substituents in 8. Release of steric strain has been found to be an important factor in determining the course of metal-halogen exchange in 2,5-dibromo-3-alkylthiophenes.[5] A pure sample of 5 was prepared by re-bromination of 7. Conversion of 7 to the acid 10 (Mg/MeI followed by CO_2) and then reduction (BH_3.THF) was found to be the most convenient route to 3. Treatment of 3 with 2.5 equivalents of n-BuLi in ether followed by CO_2 gave only a moderate yield (50%) of the acid 2 together with 27% of the lactone 11 (Scheme II). The latter must have arisen from lithiation at the 7-position followed by cyclisa-

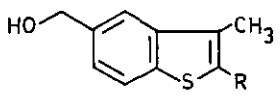
SCHEME II



tion of the hydroxy acid formed on carbonation. Since direct metalation in the benzene ring of a benzo[b]thiophene lacking a 2-substituent appears to be unprecedented it was decided to investigate the factors responsible.

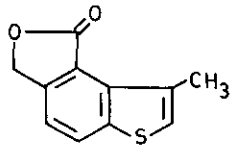
It is known that 3-methylbenzo[b]thiophene lithiates exclusively in the 2-position[6,7] so the hydroxymethyl group, in the form of its anion, must be playing a role in directing lithiation to the 7-position. The role of heteroatom substituents in complexing organolithium reagents and thereby directing lithiation in aromatic systems is now well recognised.[8] However, lithiation of benzyl alcohol in ether requires extended reaction times and even then only a low yield of product is formed after carbonation.[9,10] The more reactive n-BuLi/tetramethylethylenediamine system is required to obtain acceptable yields in this reaction.[11] Thus, it is likely that additional factors are involved in the lithiation of 3 at the 7-position. It is known that an additional heteroatom substituent in the 3-position of benzyl alcohol (e.g. OCH_3) markedly assists lithiation between the substituents.[10,15] In the case of 3, it is probable that a co-operative effect of the alkoxide anion and ring sulphur atom plays a role. The absence of any product derived from lithiation at the 5-position is evidence for the importance of the sulphur. Where metalation in the thiophene ring is not possible, as in dibenzothiophene, then the sulphur alone is sufficient to direct lithiation to an adjacent benzene ring position.[12]

In the case of the 5-hydroxymethyl compound 12, a co-operative effect is not possible, and lithiation under identical conditions followed by carbonation led to almost exclusive formation of the 2-carboxylic acid 13. Two lactone products 14 and 15 were formed in yields of only 0.8% and 1% respectively.



12, R=H

13, R=CO_2H



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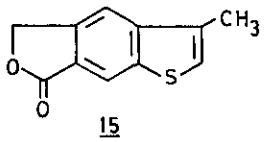

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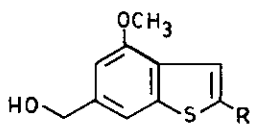
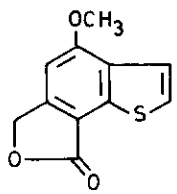
Another factor which could affect the relative extent of lithiation at the 2- and 7-positions is the inductive effect of the 3-methyl group which would decrease the acidity of the 2-proton and hence reduce the rate of lithiation relative to the corresponding desmethyl compound.[13] Thus, lithiation of 16[14] under identical conditions gave, after carbonation, a 67% yield of the 2-carboxylic acid 17 together with only 3.5% of the lactone 18 (Scheme II).

The 4-methoxy analogue 19 was considered interesting since the additional substituent might be expected to direct lithiation to the 5-position.[10,15] Treatment of 19 with n-BuLi followed by CO_2 gave a 79% yield of the 2-carboxylic acid 20. The predominant lactone product, though formed in only 0.9% yield was 21. The extent of lithiation adjacent to the methoxy group was negligible as shown by the isolation of only 0.06% of the isomeric lactone 22. The two isomers were distinguished by the presence of long range coupling (0.8 Hz) between H-3 and H-7 in the nmr spectrum of 22.[16] Thus, even when additional activation is present in the benzene ring, lithiation in the 2-position is by far the most preferred reaction.



19, R=H

20, R=CO_2H



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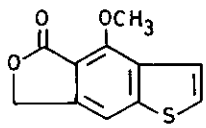

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EXPERIMENTAL

All melting points are uncorrected. The structures of all compounds were confirmed by their ir and ^1H nmr spectra. The ir spectra were recorded on a Perkin Elmer 983 spectrometer and the ^1H nmr spectra were obtained using either a Varian XL-100-15 or a Bruker WM 250 spectrometer using $CDCl_3$ as solvent unless otherwise stated. Accurate mass measurements were obtained using a VG 70 70 EHF mass spectrometer.

2,4-Dibromo-3-methylbenzo[b]thiophene (6) and 2,6-dibromo-3-methylbenzo[b]thiophene (5). Bromination of 2-bromo-3-methylbenzo[b]thiophene by the literature procedure [4] gave a mixture of 5 and 6 (85%), bp 171-173°C / 2mm., mp 35 - 40°C (lit. mp 39 - 41°C); 100 Mz ^1H nmr (5): δ 2.33 (s, 3H, CH_3), 7.44 (appr. s, 1H, H-4 or H-5), 7.45 (appr. s, 1H, H-5 or H-4), 7.82 (dd, H-7). Signals due to 6 include; 2.69 (s,3H, CH_3), 7.08 (t, 1H, J = 8Hz, H-6). The CH_3 integral ratios showed that 5 and 6 were present in the ratio 4 : 1.

4-Bromo-3-methylbenzo[b]thiophene (8) and 6-bromo-3-methylbenzo[b]thiophene (7). A 1.6M solution of n-butyllithium (93.6ml, 0.15mol) was added dropwise to a stirred solution of 5 and 6 prepared as described above (45.9g, 0.15mol) in dry ether (250ml) at 0°C. The solution was stirred at 0°C for 30 min and then an excess of water was added. The organic layer was dried (Na_2SO_4) and distilled to give a mixture of 7 and 8 (25.0g, 73%), bp 126 - 132°C/3mm (Found:C, 47.89; H, 3.10. Calc for C_9H_7BrS : C,47.59; H, 3.11%). 100MHz ^1H nmr (7) : δ 2.40 (d, 3H, J = 1.2Hz, CH_3), 7.02

(q, 1H, J = 1.2Hz, H-2), 7.46 (dd, 1H, J = 8.6, 1.7Hz, H-5), 7.53 (dd, 1H, J = 8.6, 0.7Hz, H-4), 7.95 (dd, 1H, J = 1.7, 0.7Hz, H-7). (8) : δ 2.75 (d, J = 1.2Hz, CH_3), other signals obscured.

6-Bromo-3-methylbenzo[b]thiophene (7) and 3-methylbenzo[b]thiophene-4-carboxylic acid (9). A 1.6M solution of n-butyllithium (15.2ml, 0.024mol) was added dropwise with stirring to a solution of 7 and 8 (27.5g, 0.12mol) (in a ratio 4 to 1, prepared as described above) in dry ether (200ml) at -70°C. The solution was stirred at -70° for 15 min, allowed to warm up over 30 min and then poured onto a mixture of solid CO_2 and dry ether. When the CO_2 had evaporated the mixture was washed with water and the organic layer was dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue gave 6-bromo-3-methylbenzo[b]thiophene (19.5g, 71% based on total starting material), bp 136 - 141°C / 2.5mm. Found:C, 48.00; H, 3.11. Calc for C_9H_7BrS : C,47.59; H. 3.11%. 100 MHz ^1H nmr : δ 2.40 (d, 3H, J = 1.2Hz, CH_3), 7.02 (q, 1H, J = 1.2Hz, H-2), 7.46 (dd, 1H, J = 8.6, 1.7Hz, H-5), 7.53 (dd, 1H, J = 8.6, 0.7Hz, H-4), 7.95 (dd, 1H, J = 1.7, 0.7Hz, H-7).

The aqueous layer was acidified with conc. HCl and the solid was filtered off, washed with H_2O, dried and crystallised from toluene to give 9 (3.20g, 14% based on total starting material), mp 184 - 186°C. Found:C, 62.14; H, 4.06. $C_{10}H_8O_2S$ requires: C, 62.48; H, 4.19%. 250MHz ^1H nmr $(CD_3)_2CO$: δ 2.47 (d, 3H, J = 1.3Hz, 3-CH_3), 4.35 (br s, 1H, CO_2H), 7.39 (dd, 1H, J = 7.3, 8.4Hz, H-6), 7.41 (q, 1H, J = 1.3Hz, H-2), 7.63 (dd, 1H, J = 7.3, 1.0Hz, H-5), 8.05 (dd, 1H, J = 8.4, 1.0Hz, H-7).

2,6-Dibromo-3-methylbenzo[b]thiophene (5). A solution of Br_2 (11.2g, 0.07mol) in $CHCl_3$ (50ml) was added dropwise to a stirred solution of 7 (15.9g, 0.07mol) in $CHCl_3$ (200ml). The solution was stirred for 3 h washed with H_2O, $NaHCO_3$ soln., dried (Na_2SO_4) and evaporated. Distillation of the residue gave 5 (19.0g, 89%), bp 208 - 212°C / 15 mm, mp 49 - 50°C (from petrol b.p. 40 - 60°C). Found:C, 35.88; H, 2.01. C_9H_7BrS requires: C,35.32; H. 1.98%. 100 MHz ^1H nmr : δ 2.35 (s, 3H, 3-CH_3), 7.46 (appr. s, 1H, H-4 or H-5), 7.47 (appr. s, 1H, H-5 or H-4), 7.84 (dd, 1H, H-7).

3-Methylbenzo[b]thiophene-6-carboxylic acid (10). A mixture of 7 (16.8g, 0.074mol) and iodomethane (23.8g, 0.17mol) was added dropwise to a mixture of Mg turnings (11.06g) and dry ether (150ml) at such a rate that the reaction was not too vigorous. The mixture was then heated under reflux for 30 min, cooled and poured onto a mixture of solid CO_2 and dry ether. When the CO_2 had evaporated, the mixture was washed with dil. HCl and the layers were separated. The aqueous layer was washed with ether and the combined organic layers were washed with H_2O, dried (Na_2SO_4) and evaporated. The residue was crystallised from ethyl acetate to give 10, (7.71g, 54%), mp 229 -

231°C. Found:C, 62.49; H, 4.20. $C_{10}H_8O_2S$ requires: C, 62.48; H, 4.19%. 250 MHz ^{1}H nmr $(CD_3)_2CO$: δ 2.47 (d, 3H, J = 1.0Hz, $3CH_3$), 3.75 (br s, 1H, CO_2H), 7.53 (q, 1H, J = 1.0Hz, H-2), 7.86 (dd, 1H, J = 8.4, 0.9Hz, H-4), 8.05 (dd, 1H, J = 8.4, 1.3Hz, H-5), 8.60 (dd, 1H, J = 1.3, 0.9Hz, H-7).

3-Methylbenzo[b]thiophene-5-methanol (12). A solution of ethyl 3-methylbenzo[b]thiophene-5-carboxylate (14.44g, 0.066mol) in dry ether (50ml) was added dropwise with stirring to a mixture of $LiAlH_4$ (5.32g, 0.156mol) in dry ether under dry N_2. Sufficient heat was applied during the addition to maintain gentle reflux. The mixture was heated under reflux with stirring for 3 h and then cooled. Water (5.3ml) was added cautiously with stirring, followed by 5N NaOH soln (5.3ml) and further H_2O (16ml). The mixture was filtered and the filtrate was dried (Na_2SO_4) and evaporated. The residue was crystallised from ether/petrol (bp 40 - 60°C) to give 12 (8.93g, 76%), mp 51 - 53°C. Found:C, 67.32; H, 5.66. $C_{10}H_{10}OS$ requires: C,67.38; H, 5.66%. 250 MHz ^{1}H nmr : δ 2.45 (d, 3H, J = 1.2Hz, $3CH_3$), 2.57 (s, 1H, OH), 4.79 (dd, 2H, J = 0.8, 0.5Hz, CH_2), 7.11 (dq, 1H, J = 1.2, 0.4Hz, H-2), 7.33 (dddt, 1H, J = 8.2, 1.6, 0.8, 0.4Hz, H-6), 7.67 (ddt, 1H, J = 1.6, 0.65, 0.5Hz, H-4), 7.82 (dd, 1H, J = 8.2, 0.65Hz, H-7).

3-Methylbenzo[b]thiophene-6-methanol (3). A 1M solution of borane-THF complex (44ml, 0.049mol) was added dropwise to a stirred solution of 10 (6.37g, 0.033mol) in dry THF (100ml) at 0°C. The solution was stirred at room temperature for 18 h and then an excess of MeOH was added cautiously to decompose excess borane. The solution was evaporated and the residue was dissolved in ether. The solution was washed with water, dried (Na_2SO_4), evaporated and the residue was distilled to give 3, 4.75g (81%), bp 147 - 149° / 1mm, mp 65 - 67°C (from CCl_4/petrol, bp 40 - 60°C). Found:C, 67.15; H, 5.73. $C_{10}H_{10}OS$ requires: C,67.38, H, 5.66%. 250 MHz ^{1}H nmr : δ 1.72 (s, 1H, OH), 2.44 (d, 3H, J = 1.2Hz, 3-CH_3), 4.82 (s, 2H, CH_2), 7.07 (q, 1H, J = 1.2Hz, H-2), 7.39 (dd, 1H, J = 8.2, 1.5Hz, H-5), 7.70 (dd, 1H, J = 8.2, 0.65Hz, H-4), 7.85 (dd, 1H, J = 1.5, 0.65Hz, H-7).

4-Methoxybenzo[b]thiophene-6-methanol (19). Reduction of methyl 4-methoxybenzo[b]thiophene-6-carboxylate with $LiAlH_4$ as above gave 19 (83%), mp 59.5 - 60.5°C (from ethyl acetate/petrol bp 60 - 80°C). Found:C, 61.82; H, 5.16. $C_{10}H_{10}O_2S$ requires: C,61.83; H, 5.19%. 250 MHz ^{1}H nmr: δ 1.78 (t, 1H, J = 5.95Hz, OH), 3.97 (s, 3H, OCH_3), 4.78 (d, 2H, J = 5.95Hz, CH_2), 6.78 (br s, 1H, H-5), 7.33 (d, 1H, J = 5.5Hz, H-2), 7.44 (br s, 1H, H-7), 7.47 (dd, 1H, J = 5.5, 0.7Hz, H-3).

Reaction of 3-methylbenzo[b]thiophene-6-methanol (3) with n-BuLi and CO_2. A solution of 3 (1.78g, 0.01mol) in dry ether (25ml) was added over 2 min to a stirred solution of a n-butyllithium (16.0ml of 1.6M soln in hexane, 0.025mol) in dry ether (50ml) at 0°C under dry N_2. The mixture

was stirred at 0°C for 2 h and then an excess of crushed solid CO_2 was added. When the CO_2 had evaporated, the mixture was washed with water and the aqueous extract was washed with ether and acidified with conc. HCl. The solid was filtered off, washed with water, dried at 100°C for 4 h and then partitioned between ethyl acetate and dil. $NaHCO_3$ soln. The $NaHCO_3$ layer was washed with ethyl acetate and acidified with conc. HCl. The solid was filtered off, washed with water and dried to give 2, 1.10g (50%), mp 234 - 236° (decomp.) (from ethanol/H_2O). Found:C, 59.28; H, 4.50. $C_{11}H_{10}O_3S$ requires: C,59.44; H. 4.54%. 250 MHz ^{1}H nmr ($DMSO_{d-6}$) : δ 2.72 (s, 3H, H-3), 3.36 (br s, 1H, OH), 4.66 (s, 2H, CH_2), 5.38 (br s, 1H, OH), 7.43 (dd, 1H, J = 8.4, 1.4Hz, H-5), 7.90 (dd, 1H, J = 8.4, 0.7Hz, H-4), 7.92 (dd, 1H, J = 1.4, 0.7Hz, H-7).

The combined ethyl acetate extracts were washed with water, dried (Na_2SO_4) and evaporated to give 11 (0.55g, 27%) mp 152 - 154°C (from toluene/petrol bp 60 - 80°C). Found:C, 64.42; H, 3.89. $C_{11}H_8O_2S$ requires: C,64.68; H. 3.95%. ν_{co} 1745cm^{-1}; 250 MHz ^{1}H nmr : δ 2.52 (d, 3H, J = 1.2Hz, 3-CH_3), 5.45 (d, 2H, J = 0.7Hz, CH_2), 7.27 (q, 1H, J = 1.2Hz, H-2), 7.47 (dt, 1H, J = 8.2, 0.7Hz, H-5), 8.00 (d, 1H, J = 8.2Hz, H-4).

Starting material (11%) was recovered after evaporation of the neutral ether solution.

Reaction of 3-methylbenzo[b]thiophene-5-methanol (12) with n-BuLi and CO_2. Treatment of 12 with n-BuLi and CO_2 by the above method gave the acid 13 (56%), m.p. 260 - 262°C (from ethanol). Found:C, 59.52; H, 4.70. $C_{11}H_{10}O_3S$ requires: C,59.44; H, 4.54%. 250 MHz ^{1}H nmr:($DMSO_{d-6}$) : δ 2.72 (s, 3H, 3-CH_3), 3.72 (br, OH), 4.66 (s, 2H, CH_2), 7.48 (dd, 1H, J = 8.3, 1.6Hz, H-6), 7.86 (d, 1H, J = 1.6Hz, H-4), 7.93 (d, 1H, J = 8.3Hz, H-7).

A mixture of lactones was obtained which was chromatographed on silica gel. Elution with toluene first gave 14, (0.8%), mp 179 - 180°C (from ethyl acetate). Found:C, 64.39; H, 4.08. $C_{11}H_8O_2S$ requires: C, 64.68, H, 3.95%. ν_{co} 1745cm^{-1}; 250 MHz ^{1}H nmr : δ 2.91 (d, 3H, J = 1.0Hz, CH_3), 5.38 (d, 2H, J = 0.7Hz, CH_2), 7.31 (dq, 1H, J = 0.8, 1.0Hz, H-2), 7.36 (ddt, 1H, J = 8.3, 0.8, 0.7Hz, H-6), 8.09 (d, 1H, J = 8.3Hz, H-7). Further elution with toluene gave 15 (1%), mp 197 - 198°C (from ethyl acetate). Found:C, 64.59, H, 3.90. $C_{11}H_8O_2S$ requires: C, 64.68; H, 3.95%. ν_{co} 1748 cm^{-1} ; 250 MHz ^{1}H nmr : δ 2.50 (d, 3H, J = 1.0Hz, CH_3), 5.44 (d, 2H, J = 1.0Hz, CH_2), 7.39 (q, 1H, J = 1.0Hz, 2-H), 7.77 (dt, 1H, J = 0.9, 1.0Hz, H-4), 8.40 (d, 1H, J = 0.9 Hz, H-7).

Reaction of benzo[b]thiophene-6-methanol (16) with n-BuLi and CO_2. Treatment of 16[15] with n-BuLi and CO_2 by the above method gave the acid 17 (67%), mp 220 - 222°C (from ethanol/H_2O). Found:C, 57.54; H, 3.86. $C_{10}H_8O_3S$ requires: C, 57.68; H. 3.87%. 250 MHz ^{1}H nmr (MeSO-d_6): δ 3.37 (br, 1H, OH), 4.66 (s, 2H, CH_2), 5.38 (br, 1H, OH), 7.42 (dd, 1H, J = 8.4, 1.4Hz, H-5), 7.96 (d, 1H, J = 8.4Hz, H-4), 7.97 (dd, J = 1.4, 0.7Hz, H-7), 8.07 (d, 1H, J = 0.7Hz, H-3).

The lactone 18 (3.5%) had mp 158 - 160°C (from ethyl acetate/petrol bp 60 - 80°C. M^+, m/z

190.00894. $C_{10}H_6O_2S$ requires: m/z 190.00888; ν_{CO} 1745cm^{-1}; 250MHz ^{1}H nmr : δ 5.46 (d, 2H, J = 0.7Hz, CH_2), 7.47 (dt, 1H, J = 8.1, 0.7Hz, H-5), 7.50 (d, 1H, J = 5.4Hz, H-3), 7.65 (d, 1H, J = 5.4Hz, H-2), 8.12 (d, 1H, J = 8.1Hz, H-4).

Reaction of 4-methoxybenzo[b]thiophene-6-methanol (19) with n-BuLi and CO_2. Treatment of 19 with n-BuLi and CO_2 by the above method gave the acid 20 (79%), mp 209 - 211°C (from isopropanol/petrol bp 60 - 80°C). Found:C, 55.28; H. 4.17. $C_{11}H_{10}O_4S$ requires: C, 55.45; H, 4.23%. 250 MHz ^{1}H nmr $(CD_3)_2CO$: δ 4.00 (s, 3H, OCH_3), 4.77 (dd, 2H, J = 0.9, 0.4Hz, CH_2), 6.95 (dt, 1H, J = 0.9, 0.4Hz, H-5), 7.53 (ddt, 1H, J = 0.9, 0.85Hz, H-7), 8.08 (d, 1H, J = 0.85Hz, H-3).

A mixture of lactones was obtained which was chromatographed on silica gel. Elution with ether first gave 22 (.06%), mp 130 - 132°C (from ethyl acetate). M^+, m/z 220.02004. $C_{11}H_8O_3S$ requires: m/z 220.01942; ν_{CO} 1738, 1752 cm^{-1}; 250 MHz ^{1}H nmr : δ 4.35 (s, 3H, OCH_3), 5.35 (d, 2H, J = 1.1Hz, CH_2), 7.44 (d, 1H, J = 5.55Hz, H-2), 7.56 (dt, 1H, J = 0.8, 1.1Hz, H-7), 7.62 (dd, 1H, J = 5.55, 0.8Hz, H-3).

Further elution with ether gave 21, (0.9%), mp 238 - 239°C (from ethyl acetate). Found:C, 59.77; H, 3.62. $C_{11}H_8O_3S$ requires: C, 59.98; H, 3.66%; ν_{CO} 1745, 1752 cm^{-1}; 250 MHz ^{1}H nmr : δ 4.06 (s, 3H, OCH_3), 5.37 (d, 2H, J = 0.8Hz, CH_2), 6.78 (d, 1H, J = 0.8Hz, H-5), 7.51 (dd, 1H, J = 5.5, 0.3Hz, H-2), 7.66 (d, 1H, J = 5.5Hz, H-3).

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REFERENCES

1. P.E. Cross and R.P. Dickinson, `Second SCI - RSC Med. Chem. Symposium', Royal Soc. Chem. Spec. Publn. No. 50, London, 1984, p.268.
2. H.D. Hartough and S.L. Meisel, `Compounds with Condensed Thiophene Rings', ed. A. Weissberger, Wiley (Interscience), New York, 1954.
3. B. Iddon and R.M. Scrowston, Adv. Het. Chem., 1970, 11, 177.
4. J. Cooper and R.M. Scrowston, J. Chem. Soc. (C), 1971, 3052.
5. S. Gronowitz, B. Cederlund and A-B. Hörnfeldt, Chem. Scripta, 1974, 5, 217.
6. D.A. Shirley, M.J. Danzig and F.C. Canter, J. Am. Chem. Soc., 1953, 75, 3278.
7. E. Campaigne and E.S. Neiss, J. Het. Chem., 1965, 2, 231.
8. H.W. Gschwend and H.R. Rodriguez, Org. Reactions, 1979, 26, 1.
9. H. Gilman, G.E. Brown, F.J. Webb and S.M. Spatz, J. Am. Chem. Soc., 1940, 62, 977.

10. D.J. Dodsworth, M-P. Calcagno, E.U. Ehrmann, B. Devadas and P.G. Sammes, J. Chem. Soc. Perkin I, 1981, 2120.

11. N. Meyer and D. Seebach, Chem. Ber., 1980, **113**, 1304.

12. H. Gilman and S. Gray, J. Org. Chem., 1958, **23**, 1476.

13. S. Gronowitz, Arkiv Kemi, 1954, **7**, 361.

14. Y. Matsuki and T. Kanda, Nippon Kagaku Zasshi, **86**, 1965, 637; Chem Abs. 1966, **65**, 674e.

15. B.M. Trost, G.T. Rivers and J.M. Gold, J. Org. Chem., 1980, **45**, 1835.

16. Ref. 3, p.187.

17. N.B. Chapman, K. Clarke, B.A. Gore and K.S. Sharma, J. Chem. Soc. (C), 1971, 915.

18. S.M. Abdel-Wahhab and N.R. El-Rayyes, J. Chem. Soc. (C), 1971, 3171.

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