

Substitution Reactions of 4-Methyldibenzothiophene (1)

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Succinylation, acetylation and nitration of 4-methyldibenzothiophene yields 2-substituted products. Bromination however, gave 3-bromo-4-methyldibenzothiophene as the major product along with a small amount of the 2-isomer. The bromo-compounds were used to prepare related derivatives *via* lithium exchange. 4-Methyldibenzothiophene 5,5-dioxide was also shown to nitrate in the 3-position. The structures of the derivatives were determined by NMR analyses. An alternative synthesis of 4-methyldibenzothiophene is described.

4-Methyldibenzothiophene (III) has been prepared by treatment of 4-lithiodibenzothiophene with methyl sulfate (3). Upon repeating this reaction we found that the product, even after several recrystallizations, contained dibenzothiophene (50:50 by gas liquid chromatography). An alternate synthesis previously described by Osborn (4a) and outlined in Scheme 1, involving cyclization of the keto-sulfide (I) to 1,2,3,4-tetrahydro-6-methyldibenzothiophene (II) followed by aromatization, gave superior yields of pure III. A similar sequence has been used by Tilak in the synthesis of dibenzothiophene (4b).

Succinylation, acetylation and nitration of III gave the corresponding 2-substituted products, 2-(3'-carboxypropanoyl)-4-methyldibenzothiophene (IV, X = COCH₂-CH₂COOH), 2-acetyl-4-methyldibenzothiophene (IV, X = COCH₃) and 2-nitro-4-methyldibenzothiophene (IV, X = NO₂), respectively. The 100 MHz NMR spectra of some substituted dibenzothiophenes have recently been reported by us (5). The introduction of the 4-methyl group in the present compounds results in a simplification of the NMR spectra. The above products were clearly shown to be 2-substituted by the presence of broadened singlets for H-1 and H-3, both being shifted to low field due to the *ortho* effect of the electron withdrawing substituents. Shifts are measured from the center of the multiplet given by the corresponding proton in the unsubstituted ring (5). These assignments were confirmed by the presence of a small (*ca.* 2 Hz) *meta*-coupling between the resonances of H-1 and H-3.

Bromination of III gave a mixture of 3-bromo-4-methyldibenzothiophene (V, X = Br, 30%) and 2-bromo-4-methyldibenzothiophene (IV, X = Br, 3%). The structures of these products were not readily determined from their NMR spectra due to the unpredictable shielding or deshielding effect of the bromo substituent upon adjacent protons.

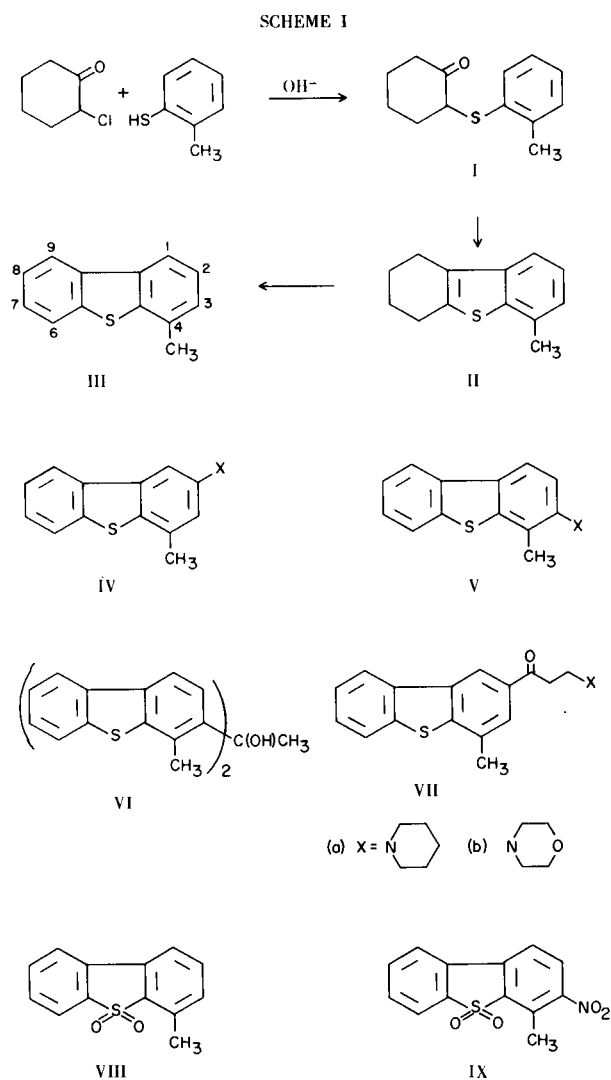
The bromo-compounds were therefore converted to the corresponding aldehydes by treatment with butyllithium and *N,N*-dimethylformamide, yielding 3-formyl-4-methyldibenzothiophene (V, X = CHO) and 2-formyl-4-methyldibenzothiophene (IV, X = CHO), respectively. The position of substitution was then readily determined from the NMR spectra of the aldehydes. The spectrum of V (X = CHO) gave two doublets (*J* = 9 Hz) at δ 7.98 and δ 7.78 associated with H-1 and H-2. The H-1 doublet occurred along with the H-9 multiplet while the H-2 doublet was deshielded by 32 Hz, from the H-7,8 multiplet. The 4-methyl resonance of V (X = CHO) occurred at δ 2.82, being 40 Hz lower field than in 4-methyldibenzothiophene (δ 2.42), again consistent with the presence of formyl group *ortho* to the methyl group. The spectrum of IV (X = CHO) clearly showed 2-substitution by the presence of singlets at δ 8.21 and 7.59 associated with H-1 and H-3, respectively. The resonance of the 4-methyl group in this compound occurred at δ 2.49. Further confirmation of the structures of the aldehydes was afforded by the spectrum of 3,4-dimethyldibenzothiophene (V, X = CH₃) formed by Wolff-Kishner reduction of V (X = CHO) where the 4-methyl resonance reverted from δ 2.82 in V (X = CHO) to δ 2.33 in V (X = CH₃).

Treatment of V (X = CHO) under Cannizzaro conditions yielded 3-hydroxymethyl-4-methyldibenzothiophene (V, X = CH₂OH). Reaction of the lithio compound derived from V (X = Br) with carbon dioxide gave 3-carboxy-4-methyldibenzothiophene (V, X = COOH). Reaction of 3-lithio-4-methyldibenzothiophene with ethyl acetate furnished the bis-alcohol (VI). A similar reaction was observed with 2-bromodibenzothiophene (5). The structure of VI was established by elemental analysis and the determination of its mass spectrum as well as analogy to the

dibenzothiophene case.

2-Acetyl-4-methyldibenzothiophene (IV, X = COCH₃) underwent the Mannich reaction with piperidine and morpholine to yield to expected Mannich bases (VII, X = *N*-piperidyl and *N*-morpholyl).

Oxidation of III with hydrogen peroxide in acetic acid gave 4-methyldibenzothiophene 5,5-dioxide (VIII) (4). Attempts to isolate the corresponding sulfoxide by reducing the reaction time were unsuccessful. Nitration of VIII yielded 4-methyl-3-nitrodibenzothiophene 5,5-dioxide, (IX) (6).



This change in the nitration position from 2- to 3- upon oxidizing the sulfur atom parallels the behaviour of dibenzothiophene upon oxidation (7). The structure of IX was established from its NMR spectrum (dimethylsulfoxide) which exhibited two doublets ($J = 8$ Hz) at

δ 8.6 and 8.76. This is consistent with H-2 being deshielded by the nitro-group to approximately the same chemical shift as the H-1 resonance. The 4-methyl resonance occurred at δ 3.14. A comparison of the methyl resonances in deuteriochloroform of III, VIII and IX revealed that the methyl group is deshielded in 4-methyldibenzothiophene 5,5-dioxide (VIII, δ 2.69) compared with 4-methyldibenzothiophene (III, δ 2.42), as would be expected. Moreover the methyl resonance in 4-methyl-3-nitrodibenzothiophene 5,5-dioxide (IX, δ 2.94) is deshielded by a further 25 Hz consistent with an *ortho*-related (3-position) nitro group.

Confirmation of the assignment of resonances in the NMR spectrum of dibenzothiophene made by Faller (8) was afforded by a decoupling experiment carried out upon 2-acetyl-4-methyldibenzothiophene (IV, X = COCH₃). Irradiation at δ 7.43, the center of the H-7,8 multiplet caused the H-9 multiplet at δ 8.11 to collapse to a singlet, consistent with the accepted assignments of these multiplets. In a further attempts to confirm the assignment of the multiplets given by dibenzothiophene, the method of Johnson and Bovey (9) was used to calculate the effect of the ring current of one ring upon the deshielding of protons in the other ring. This gave predicted values for the proton resonances as follows: H-1,9, δ 7.7, H-4,6, 7.5 and H-2,3,7,8, 7.4. These values are in the correct order (observed δ 8.0, 7.7 and 7.3 respectively) but are not large enough. It therefore seems probable that this effect is further enhanced by low electron densities at C-1,9 and C-4,6 due to the sulfur atom.

EXPERIMENTAL

Melting points were determined on a Mel-Temp melting point apparatus and are corrected. Infrared spectra were measured in potassium bromide mulls on an Infracord Model 137-B Spectrometer. The 100 MHz NMR spectra were determined in deuteriochloroform, unless otherwise stated, on a Varian HA-100 instrument at 20°, tetramethylsilane being used as internal standard. Ether solutions were dried with anhydrous magnesium sulfate. The butyllithium used was a commercially available 15% solution in hexane.

In reporting the NMR the following abbreviations have been used: s = singlet; d = doublet; dd = double doublet; m = multiplet. δ Values for multiplets represent the center of the resonances.

2-(*o*-Tolythio)cyclohexanone (I).

o-Thiocresol (62 g., 0.50 mole) and sodium hydroxide (20 g., 0.50 mole) were heated under reflux with ethanol (75 ml.) and water (75 ml.). 2-Chlorocyclohexanone (65.0 g., 0.505 mole) dissolved in ethanol (75 ml.) was added dropwise to the refluxing mixture during 15 minutes and reflux was continued for 1.5 hours. The mixture was cooled and shaken with 1800 ml. of water; the lower, oily layer was removed, and the aqueous phase was extracted with ether (4 x 200 ml.). The oil and extracts were combined, washed with water (50 ml.), dried, and the ether was evaporated leaving a yellow oil which was distilled under reduced pressure.

The main fraction was collected as a viscous, light yellow oil, b.p. 121-121.5° at 0.15 mm. (93 g., 85%).

The oil was characterized by its 2,4-dinitrophenylhydrazone which was recrystallized from ethanol-ethyl acetate, m.p. 144-144.5°.

Anal. Calcd. for C₁₉H₂₀N₄O₄S: C, 57.0; H, 5.03. Found: C, 57.3; H, 4.86.

1,2,3,4-Tetrahydro-6-methyldibenzothiophene (II).

Polyphosphoric acid (150 g.) was added to *o*-tolylthiocyclohexanone at 200-210° and the mixture was stirred at ca. 200° for 1 hour. The mixture was then poured into ice (200 g.) and allowed to stand for several hours. The oily layer was separated, the aqueous phase was extracted with ether (2 x 100 ml.), and the oil and extracts were combined and washed with a 5% sodium bisulfite solution and water. The ether solution was dried, the solvent was evaporated, and the residue was distilled under reduced pressure to give a main fraction, b.p. 132-134° at 0.6 mm. (14.1 g., 70%) as a colorless oil.

The product was characterized as its picrate which was recrystallized from ethanol, m.p. 96.5-97°.

Anal. Calcd. for C₁₉H₁₇N₃O₇S: C, 52.9; H, 3.97. Found: C, 53.2; H, 3.79.

4-Methyldibenzothiophene (III).

A mixture of II (16.2 g., 0.080 mole) and powdered selenium (15.8 g., 0.20 mole) were heated to 300° in a small flask fitted with a condenser, using a Wood's metal bath. From the top of the condenser a rubber tube was connected to a glass tower filled with chlorinated lime. Hydrogen selenide was evolved as evidenced by the progressive red coloration of the lime. After approximately 8 hours when hydrogen selenide evolution had ceased, the flask was cooled and the contents were repeatedly extracted with hot ethanol. The hot alcoholic solution was treated with activated carbon, concentrated, and cooled, affording the product as plates (15.0 g., 95%), m.p. 64.5°. A further recrystallization raised the m.p. to 66-66.5°; NMR δ 7.8 (m, H-1,6,9), 7.2 (m, H-2,3,7,8), 2.42 (s, 4-CH₃).

Anal. Calcd. for C₁₃H₁₀S: C, 78.8; H, 5.08. Found: C, 78.5; H, 5.03.

The picrate of 4-methyldibenzothiophene was prepared and recrystallized from ethanol, m.p. 110-110.5°.

Anal. Calcd. for C₁₉H₃O₇S: C, 53.4; H, 3.07. Found: C, 53.4; H, 3.13.

2-(3'-Carboxypropanoyl)-4-methyldibenzothiophene (IV, X = COCH₂CH₂COOH).

A mixture of III (39.6 g., 0.20 mole) succinic anhydride (21.0 g., 0.21 mole), and *sym*-tetrachloroethane was heated and 25 ml. of the solvent was distilled to remove traces of moisture in the system. The mixture was cooled to -5° and a solution of anhydrous aluminum chloride (56.0 g., 0.42 mole) in dry nitrobenzene (100 ml.) was added dropwise with stirring over 4 hours. After standing at 0° for 20 hours the solution was poured with stirring into a mixture of ice (1 kg.) and 38% hydrochloric acid (75 ml.). The mixture was allowed to stand overnight, the aqueous layer was decanted, and the organic layer was steam distilled. The aqueous layer was again decanted, the organic layer was shaken with a 10% aqueous sodium carbonate solution (300 ml.), and steam distilled for 30 minutes. The alkaline solution was cooled, filtered, and acidified with 18% hydrochloric acid, and the resulting precipitate was collected, washed with water, air-dried, and crystallized from redistilled cyclohexanone (36.5 g., 61%, m.p. 231-234°). An analytical sample from an excess of

benzene had m.p. 235-235.5°; IR 3.27, 5.87 (acid C=O), 5.98 (ketone C=O), 6.30, 7.10 μ ; NMR (dimethylsulfoxide external TMS standard) δ 8.81 (s, H-1), 8.50 (m, H-9), 8.08 (m, H-6), 7.91 (s, H-3), 7.55 (m, H-7,8), 3.44 and 2.68 (t,t, aliphatic CH₂, J = 7 Hz), 2.58 (s, 4-CH₃).

Anal. Calcd. for C₁₇H₁₄O₃S: C, 68.4; H, 4.73. Found: C, 68.3; H, 4.63.

2-Acetyl-4-methyldibenzothiophene (IV, X = COCH₃).

Aluminum chloride (60.6 g., 0.455 mole) in nitrobenzene (200 ml.) was added with stirring to a solution of III (30.00 g., 0.151 mole) and acetyl chloride (12.8 g., 11.06 ml., 0.154 mole) in dry nitrobenzene (400 ml.) at 2° over 1 hour. The resulting solution was stirred at 4° for 42 hours before adding ice (400 g.). The mixture was steam distilled for 6 hours and the remaining aqueous mixture was extracted with ether (3 x 300 ml.), the ether layers were combined, dried, and the solvent was evaporated leaving a brown gum which hardened upon standing (32.4 g., 90%). The product was crystallized from an excess of cyclohexane. The solution was decanted from small amounts of a dark oil which separated, and after refrigeration afforded 13.9 g. of crude IV (X = COCH₃). A further crystallization from methanol gave 11.9 g. (33%) m.p. 110-113°. The analytical sample had m.p. 120-120.5°; IR 3.28, 6.01 (C = O), 6.30, 7.06 μ ; NMR δ 8.42 (3, J_{1,3} = 1 Hz, H-1), 8.05 (m, H-9), 7.72 (m, H-6), 7.73 (d, J_{3,1} = 1 Hz, H-3), 7.38 (m, H-7,8), 2.50 (s, 4-CH₃), 2.63 (s, 2-COCH₃).

Anal. Calcd. for C₁₅H₁₂OS: C, 75.0; H, 5.03; S, 13.3. Found: C, 74.8; H, 4.96; S, 13.1.

2-Acetyl-4-methyldibenzothiophene Oxime (IV, X = CNOHCH₃).

2-Acetyl-4-methyldibenzothiophene (2.00 g., 0.00833 mole) was added to a mixture of hydroxylamine hydrochloride (5.00 g.) and a 10% aqueous solution of sodium hydroxide (20 ml.). Ethanol was added until the refluxing solution clarified (120 ml.). After refluxing for 20 minutes, water (50 ml.) was added to precipitate the product. Cooling the solution afforded a powder, m.p. 170-174° which was crystallized from ethanol-water as needles (1.76 g., 83%), m.p. 177-178°; IR 3.12 (OH), 7.07, 10.45, 11.11 μ (unassigned).

Anal. Calcd. for C₁₅H₁₃NOS: C, 70.6; H, 5.13; S, 12.5. Found: C, 70.7; H, 5.19; S, 12.3.

2-Nitro-4-methyldibenzothiophene (IV, X = NO₂).

Nitric acid (3.0 ml., sp. gr. 1.50) was added with stirring to a solution of III (3.00 g., 0.0151 mole) in glacial acetic acid (25 ml.) at 30° over a period of 10 minutes. The mixture was stirred at room temperature for an additional 50 minutes and then poured over ice (150 g.). The aqueous phase was decanted, and the remaining gummy, yellow solid was washed and crystallized from 95% aqueous ethanol as a yellow powder (1.37 g., 37%, m.p. 119.5-131.5°). A further recrystallization from methanol-water afforded 0.96 g. of the product (26%), m.p. 138-145°; IR 6.35, 6.68 (nitro), 6.83, 7.56 μ ; NMR δ 8.82 (d, J_{1,3} = 2 Hz, H-1), 8.18 (m, H-9), 8.12 (d, J_{3,1} = 2 Hz, H-3), 7.90 (m, H-6), 7.56 (m, H-7,8), 2.68 (s, 4-CH₃). An analytical sample, m.p. 150.5-152°, from another run was otherwise identical.

Anal. Calcd. for C₁₃H₉NO₂S: C, 64.2; H, 3.73; S, 13.2. Found: C, 64.2; H, 3.90; S, 13.4.

3-Bromo-4-methyldibenzothiophene (V, X = Br).

A solution of III (113.0 g., 0.571 mole) in carbon disulfide (1.13 l.) was cooled to 0° and bromine (91.5 g., 0.571 mole, 32.1 ml.) in carbon disulfide (30 ml.) was added dropwise with stirring over 30 minutes. The resulting solution was allowed to

stand for 72 hours, and the solvent was evaporated leaving a red-brown oil which solidified upon standing. Recrystallization from petroleum ether (30-60°) afforded fine plates (54.0 g., 34%, m.p. 110-115°). A further recrystallization gave 46.7 g. (30%), m.p. 132-133° from several crops of plates obtained by successive reductions in the volume of solvent. The analytical sample had m.p. 134-135.5°; IR 6.36, 7.00, 7.31, 12.24. μ ; NMR δ 7.98 (m, H-9), 7.73 (m, H-6), 7.70 (d, $J_{1,2} = 9$ Hz, H-1), 7.52 (d, $J_{2,1} = 9$ Hz, H-2), 7.38 (m, H-7,8), 2.62 (s, 4-CH₃).

Anal. Calcd. for C₁₃H₉BrS: C, 56.3; H, 3.27; Br, 28.8. Found: C, 56.0; H, 3.24; Br, 29.1.

2-Bromo-4-methyldibenzothiophene (IV, X = Br).

The mother liquor from the above first recrystallization was reduced to dryness, and the oily residue distilled. The main fraction had b.p. 135-175° (0.3 mm. Hg) and was collected as a clear liquid which crystallized upon standing (66.0 g.). Dissolving this in 1 l. of hot petroleum ether (30-60°) and cooling at 4° for 2 days gave plates (2.65 g., m.p. 116-127°). Reducing the volume of the mother liquor and further cooling for 2 days afforded a further 6.32 g. of the solid, m.p. 110-119°. Recrystallization of these combined solids from hexane raised the m.p. to 135.5-137.5° (6.00 g.). This material was identified as 3-bromo-4-methyldibenzothiophene. Evaporation of the petroleum ether residues from the crystallization of the above distillate left an oil which partially crystallized upon standing. Shaking the mixture with cold petroleum ether and filtering gave crystals, 6.31 g., m.p. 94.5-95.5°. Recrystallization from methanol gave long needles of IV (X = Br) (4.50 g., 3%, m.p. 100-101.5°); IR 6.40, 7.11, 11.83 μ ; NMR δ 8.01 (s, H-1), 7.96 (m, H-9), 7.77 (m, H-6), 7.42 (s, H-3), 7.35 (m, H-7,8), 2.47 (s, 4-CH₃).

Anal. Calcd. for C₁₃H₉BrS: C, 56.3; H, 3.27; Br, 28.8. Found: C, 56.3; H, 3.22; Br, 29.0.

4-Methyldibenzothiophene-3-carboxaldehyde (V, X = CHO).

Butyllithium (37.5 ml., 0.62 mole) was added to a solution of V (X = Br) (15.00 g., 0.0542 mole) in sodium-dry ether (400 ml.) cooled to 0°. The solution was stirred for 2 minutes and *N,N*-dimethylformamide (3.95 g., 4.20 ml. 0.0542 mole) in ether (5 ml.) was added. After refluxing for 1 hour, the mixture was hydrolyzed by pouring it over a mixture of ice (300 g.) and 38% hydrochloric acid (15 ml.). The organic layer was separated and the aqueous layer extracts were dried and evaporated leaving a fluffy powder (12.20 g., 99%, m.p. 93-103°). Recrystallization from 95% ethanol raised the m.p. to 109-110°, (10.13 g., 83%); IR 5.97 (C=O), 6.33, 7.29, 8.14 μ ; NMR δ 10.66 (s, CHO), 8.08 (m, H-9), 7.98 (d, $J_{1,2} = 9$ Hz, H-1), 7.82 (m, H-6), 7.78 (d, $J_{2,1} = 9$ Hz, H-2), 7.46 (m, H-7,8), 2.82 (s, 4-CH₃).

Anal. Calcd. for C₁₄H₁₀OS: C, 74.3; H, 4.45; S, 14.2. Found: C, 74.0; H, 4.63; S, 14.0.

4-Methyldibenzothiophene-2-carboxaldehyde (IV, X = CHO).

This was prepared from compound IV (X = Br) by the method given above for the 3-isomer. The crude product (92%) crystallized from methanol as needles (77%), m.p. 88.5-90.5°. A further recrystallization raised the m.p. to 93-93.5°; IR 5.96 (C=O), 6.31, 7.56, 13.24 μ (unassigned); NMR δ 9.96 (s, CHO), 8.21 (s, H-1), 8.03 (m, H-9), 7.74 (m, H-6), 7.59 (s, H-3), 7.42 (m, H-7,8), 2.49 (s, 4-CH₃).

Anal. Calcd. for C₁₄H₁₀O₂S: C, 74.3; H, 4.45. Found: C, 74.1; H, 4.60.

3,4-Dimethyldibenzothiophene (V, X = CH₃).

A mixture of V (X = CHO) (5.00 g., 0.00221 mole) and

hydrazine hydrate (88% aqueous solution, 1.44 ml.) in diethylene glycol (5 ml.) was heated on a Wood's metal bath at 160° for 15 minutes, cooled to 60° and finely ground sodium hydroxide (0.446 g.) was added. The resulting solution was refluxed for 1.5 hours, poured into ice water (150 ml.), extracted with ether (2 x 50 ml.) and the combined ether extracts were dried. Evaporation of the solvent gave the product as an off-white solid which crystallized from methanol-water as fine needles, m.p. 66.5-69.5° (0.310 g., 66%). Two further recrystallizations gave material of analytical purity, m.p. 70.5-71.5°; IR 3.45, 6.97, 12.25, 13.28 μ ; NMR δ 7.93 (m, H-9), 7.73 (d, $J_{1,2} = 9$ Hz, H-1), 7.70 (m, H-6), 7.29 (m, H-7,8), 7.08 (d, $J_{2,1} = 9$ Hz, H-2), 2.38 (s, 3-CH₃), 2.33 (s, 4-CH₃).

Anal. Calcd. for C₁₄H₁₂S: C, 79.2; H, 5.70; S, 15.1. Found: C, 79.2; H, 5.71; S, 14.8.

3-Hydroxymethyl-4-methyldibenzothiophene (V, X = CH₂OH).

A 50% aqueous solution of sodium hydroxide (15 ml.) was added to V (X = CHO) (2.00 g., 0.00885 mole) and ethanol (7 ml.) and the resulting solution was refluxed for 5 hours. The orange colored mixture was poured into water (15 ml.) and heated to remove the ethanol. Ether (200 ml.) was added, the suspension was stirred, filtered, the ether phase was separated and the aqueous layer was extracted with ether (2 x 25 ml.). The combined ether extracts were dried and the solvent was evaporated leaving the product as an orange powder (0.82 g., 82%, m.p. 109.5-117.5° which was crystallized from benzene as needles (0.45 g., 45%, m.p. 122.5-123.5°); IR 3.05 (hydroxyl), 6.38 and μ 6.99. An analytical sample from petroleum ether (60-90°) had m.p. 130.5-131.5°.

Anal. Calcd. for C₁₄H₁₂OS: C, 73.7; H, 5.29; S, 14.0. Found: C, 73.8; H, 5.34; S, 13.7.

4-Methyldibenzothiophene-3-carboxylic Acid (V, X = COOH).

Butyllithium (2.40 ml., 0.00400 mole) was added to a solution of V (X = Br) (1.00 g., 0.00361 mole) in sodium-dry ether (25 ml.) cooled to 0° under an atmosphere of dry nitrogen and the resulting solution was stirred for 2 minutes. An excess of solid carbon dioxide was added and the solution was stirred at room temperature for 5 minutes before pouring it over a mixture of ice (50 g.) and 38% hydrochloric acid (3 ml.). The free acid was dissolved in ether, the ether layer was separated and the aqueous phase was extracted with ether (2 x 30 ml.). The combined ether extracts were dried and the solvent was evaporated leaving a fluffy powder (0.80 g., (92%), m.p. 244.5-245°) which upon crystallization from ethanol-water gave 0.73 g. (84%), of V (X = COOH), m.p. 246-246.5°; IR 5.97 (C=O), 7.87, μ 13.41.

Anal. Calcd. for C₁₄H₁₀O₂S: C, 69.4; H, 4.16; S, 13.2. Found: C, 69.2; H, 4.20; S, 13.2.

Bis-3-(4-Methyldibenzothiophenyl)methylcarbinol (VI).

To a solution of V (X = Br) (1.00 g., 0.00361 mole) in sodium-dry ether (25 ml.) cooled to 0° was added butyllithium (2.40 ml., 0.00400 mole) and the resulting solution was stirred for 2 minutes before adding ethyl acetate (0.317 g., 0.00361 mole, 0.353 ml.). The mixture was refluxed for 2 hours and poured into water (25 ml.). The organic phase was separated and the aqueous phase was extracted with ether (2 x 20 ml.). The combined ether extracts were dried and the solvent evaporated leaving a yellow solid (0.80 g.) which was crystallized from benzene as fine needles, 0.33 g. (43%), m.p. 192-194°. Two further recrystallizations raised the m.p. to 203-204.5°; IR 2.92 (OH), 6.94, 7.30 μ ; MW Calcd. 438. Found (mass spectrum) 438.

Anal. Calcd. for $C_{28}H_{22}OS_2$: C, 76.7; H, 5.06. Found: C, 77.1; H, 5.29.

2-(3'-*N*-Piperidylpropanoyl)-4-methyldibenzothiophene Hydrochloride (VIIa-HCl).

To piperidine (0.107 g., 0.00125 mole, 0.136 ml.) in absolute ethanol (0.7 ml.) was added 38% hydrochloric acid until the pH was 3-4. Then 2-acetyl-4-methyldibenzothiophene (0.300 g., 0.00125 mole) and paraformaldehyde (0.053 g.) were added and the resulting solution was refluxed for 5 hours. The mixture was poured into 4 ml. of dry acetone and cooled overnight giving 0.25 g. of a powder (56%), m.p. 193-205°. Recrystallization from 95% ethanol gave the product as needles (0.185 g., 45%, m.p. 199-203°); IR 3.79, 3.92 (NRH⁺), 5.97 (C=O), 6.27 μ . An analytical sample from ethanol had m.p. 204-205°.

Anal. Calcd. for $C_{21}H_{24}ClNOS$: C, 67.5; H, 6.47; N, 3.75. Found: C, 67.3; H, 6.72; N, 3.87.

2-(3'-*N*-Morpholinylpropanoyl)-4-methyldibenzothiophene Hydrochloride (VIIb-HCl).

To morpholine (0.723 g., 0.00833 mole, 0.723 ml.) in absolute ethanol (4.5 ml.) was added 38% hydrochloric acid until the pH was 3-4. Then 2-acetyl-4-methyldibenzothiophene (2.00 g., 0.00833 mole) and paraformaldehyde (0.39 g.) were added and the resulting solution was refluxed for 4 hours. The clear solution was poured into acetone (20 ml.) and cooled in the refrigerator overnight affording the product as off-white crystals (1.52 g., 52%), m.p. 204-206°. An analytical sample from ethanol had m.p. 204-205.5°.

Anal. Calcd. for $C_{20}H_{22}ClNO_2S$: C, 63.9; H, 5.92; N, 3.73. Found: C, 63.7; H, 5.97; N, 3.60.

4-Methyldibenzothiophene 5,5-Dioxide (VIII).

Hydrogen peroxide (30% aqueous, 14.4 ml.) was added to a solution of III (5.00 g., 0.254 mole) in glacial acetic acid (19 ml.) at 90° and the mixture was stirred under reflux for 1.5 hours. The mixture was kept overnight at room temperature and the resultant precipitate was collected by filtration, washed with water and dried. Crystallization from benzene gave the product as a colorless powder (3.85 g., 66%), m.p. 170-172°. An analytical sample from benzene had m.p. 178-179°; IR 6.30 and 6.95 (aromatic C=C), 7.85 and 8.70 μ (sulfone); NMR δ 7.12-7.90 (m, aromatic H's), 2.69 (s, 4-CH₃).

Anal. Calcd. for $C_{13}H_{10}O_2S$: C, 67.8; H, 4.37; S, 13.9. Found: C, 67.4; H, 4.47; S, 13.7.

3-Nitro-4-methyldibenzothiophene 5,5-Dioxide (IX).

A solution of VIII (12.6 g., 0.0543 mole) in a mixture of glacial acetic acid (25.7 ml.) and concentrated sulfuric acid (25.7 ml.) was placed in a 250 ml. flask equipped with a stirrer, thermometer, and dropping funnel. The solution was stirred at 4° while nitric acid (sp. gr. 1.5, 27.6 ml.) was added over 1.25 hours. The resultant solution was stirred for a further 0.5 hour and then poured into water (250 ml.). The resultant yellow solid was filtered and washed with water. Crystallization from 1,4-dioxane gave the product as light red needles (2.5 g., 17%), m.p. 270-272°. An analytical sample had m.p. 276-277°; IR 6.6 and 7.5 (nitro), 7.8 and 8.7 μ (sulfone); NMR (dimethylsulfoxide, tetramethylsilane as external standard) δ 8.76 and 8.60 (d, J = 9 Hz, H-1,2), 8.65 (m, H-9), 8.43 (m, H-6), 8.20 (m, H-7,8), 3.14 (s, 4-CH₃). In deuteriochloroform the 4-CH₃ resonance occurred at δ 2.94.

Anal. Calcd. for $C_{13}H_9NO_4S$: C, 56.8; H, 3.30; N, 5.09; S, 11.7. Found: C, 56.9; H, 3.36; N, 5.09; S, 11.8.

REFERENCES

- (1) Contribution No. 1718, supported by Public Health Service Research Grant GM-10366 to Indiana University.
- (2) Taken in part from the Master of Science thesis of L. H., to be submitted to Indiana University, June, 1969.
- (3) H. Gilman and A. L. Jacoby, *J. Org. Chem.*, **3**, 108 (1938).
- (4a) S. W. Osborn, Ph.D. thesis, Indiana University, 1962; (b) K. Rabinran and B. D. Tilak, *Current Science* (India), **20**, 207 (1951).
- (5) E. Campaigne, J. Ashby, *J. Heterocyclic Chem.*, **6**, 517 (1969).
- (6) We are indebted to D. McClure, Indiana University, for preparation of this compound.
- (7) R. K. Brown, R. K. Christiansen and R. B. Sandin, *J. Am. Chem. Soc.*, **70**, 1748 (1948).
- (8) P. Faller, *Bull. Soc. Chim. France*, 387 (1967).
- (9) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, **29**, 1956 (1958).

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