135. *Synthesis of Naphtho*[2,3-b]*thiophen.*

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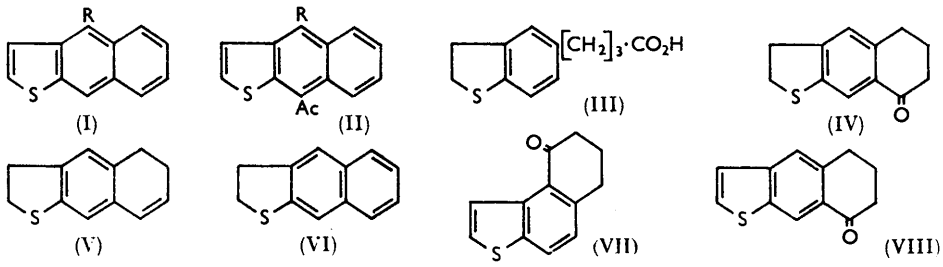
Naphtho[2,3-*b*]thiophen has been prepared by way of its 4-acetoxy-derivative which was obtained from *o*-2-thenylbenzoic acid. In a second method, the acid (III) was cyclised to the ketone (IV) from which naphtho-[2,3-*b*]thiophen was obtained by reduction of the carbonyl group and dehydrogenation. Several side-reactions are also mentioned.

In view of the difficulty of obtaining naphtho[2,3-*b*]thiophen (I; R = H) by reduction of the quinone,[1] we investigated alternative routes.

o-2-Thenoylbenzoic acid [2] was reduced with zinc dust and ammonia to *o*-2-thenylbenzoic acid, which was smoothly converted with zinc chloride in acetic acid and acetic anhydride [3] into 4-acetoxynaphtho[2,3-*b*]thiophen (I; R = OAc). Reduction of this compound with zinc dust and sodium hydroxide or with tricyclohexyloxyaluminium in cyclohexanol [4] afforded naphtho[2,3-*b*]thiophen in excellent yield. The structure was confirmed by oxidation to the quinone, and by desulphurisation with Raney nickel [5] to 2-ethylnaphthalene. A minor product of the cyclisation was the acetoxy-derivative (II; R = OAc). On oxidation with chromic acid it afforded the 4,9-quinone, and on treatment with dimethyl sulphate and alkali it was converted into the methoxy-derivative (II; R = OMe).

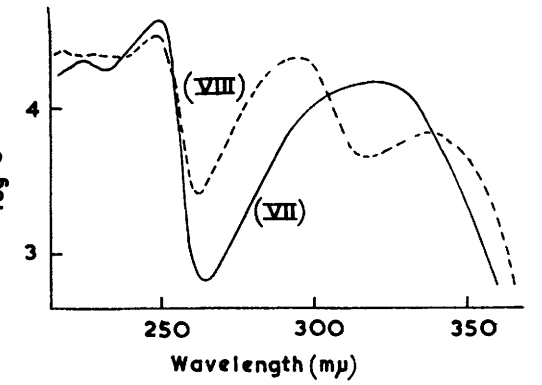


In another approach the acid (III) was conveniently prepared by Friedel–Crafts condensation of 2,3-dihydrobenzo[*b*]thiophen with succinic anhydride, and reduction of the carbonyl group by Huang-Minlon's procedure.[6] The orientation of the side chain was established by desulphurisation with Raney nickel and oxidation of the product to isophthalic acid. Treatment of the acid chloride of (III) with stannic chloride afforded an oily mixture of ketones but with hydrofluoric acid the crystalline ketone (IV) was obtained in good yield, whence reduction of the carbonyl group and dehydrogenation with sulphur gave the desired naphtho[2,3-*b*]thiophen (I; R = H). A small amount of a dihydro-compound $C_{12}H_{10}S$ was invariably produced in this dehydrogenation, and also when the tetrahydro-compound (V) was used, or when dehydrogenation was effected with chloranil in boiling xylene. The dihydro-compound afforded (I; R = H) on further dehydrogenation, and it is formulated as (VI) because of the similarity of its ultraviolet absorption spectrum to that of methyl 2-naphthyl sulphide. Some support for this is provided by the nuclear magnetic resonance spectrum (kindly determined by Dr. L. M. Jackman);

[1] Steinkopf, *Annalen*, 1915, **407**, 94; Carruthers and Crowder, *J.*, 1957, 1932; but see Wilputte and Martin, *Bull. Soc. chim. belges*, 1956, **65**, 874.
[2] Goncalves and Brown, *J. Org. Chem.*, 1952, **17**, 698.
[3] Compare, Fieser, and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 1028.
[4] Coffey and Boyd, *J.*, 1954, 2468.
[5] Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013; Blicke and Sheets, *ibid.*, 1948, **70**, 3768; 1949, **71**, 4010.
[6] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487, and later papers.

there is no peak at values of τ above 4 corresponding to styrene-type protons of possible alternative formulations [*e.g.* (V) with double bond between $C_{(2)}$ and $C_{(3)}$].

By dehydrogenation of the methyl ester of acid (III), and hydrolysis, the corresponding benzo[*b*]thienylbutyric acid was obtained. Cyclisation by treatment of the acid chloride with stannic chloride afforded mainly the ketone (VII), identified by its conversion into naphtho[2,1-*b*]thiophen, and another ketone regarded as the alternative cyclisation product (VIII). It is of interest that the ultraviolet absorption spectra of (VII) and



Ultraviolet absorption spectrum of 4-oxo-4,5,6,7-tetrahydronaphtho[2,1-*b*]thiophen (VII) and of 8-oxo-5,6,7,8-tetrahydronaphtho[2,3-*b*]thiophen (VIII).

(VIII) are differentiated in the same way as those of 1- and 2-acylnaphthalenes; [7] the spectrum of the ketone (VII) shows only two regions of absorption as is general for 1-acylnaphthalenes, while the ketone (VIII) resembles 2-acylnaphthalenes in having three groups of bands (see Fig.).

Experimental

Ultraviolet spectra refer to solutions in 95% ethanol unless otherwise stated.

o-2-*Thenylbenzoic Acid.*—A solution of *o*-2-thenoylbenzoic acid [2] (9·2 g.) in 50% ammonia (500 c.c.) was boiled with zinc dust (30 g.) for 48 hr. Excess of zinc was filtered off, and the *product* recovered from the acidified filtrate. It crystallised from dilute ethanol as needles (3·3 g.), m. p. 102—103° (Found: C, 66·1; H, 4·6. $C_{12}H_{10}O_2S$ requires C, 66·0; H, 4·6%).

4-*Acetoxynaphtho*[2,3-b]*thiophen.*—A solution of the above acid (3·3 g.) and zinc chloride (0·3 g.) in acetic acid (30 c.c.) and acetic anhydride (20 c.c.) was boiled for 1 hr. Water was added until a faint turbidity appeared, and the solution was set aside. 4-*Acetoxynaphtho*-[2,3-b]*thiophen* (2·5 g.) separated and recrystallised from cyclohexane as very pale yellow needles, m. p. 119—120° (Found: C, 69·4; H, 4·1. $C_{14}H_{10}O_2S$ requires C, 69·4; H, 4·2%), $\lambda_{max.}$ 250, (317), (327), 339, 356 mμ (log ε 4·85, 3·64, 3·75, 3·82, 3·89).

4-*Acetoxy*-9-*acetylnaphtho*[2,3-b]*thiophen.*—Further dilution with water of the acetic acid mother liquors from the above reaction afforded a crude green product (800 mg.). Chromatography on alumina and elution with benzene–light petroleum (b. p. 60—80°) (1 : 1) gave first the acetoxy-compound and then the *acetoxyacetyl derivative* which crystallised from cyclohexane as pale yellow blades, m. p. 142—143° (Found: C, 67·6; H, 4·3. $C_{16}H_{12}O_3S$ requires C, 67·6; H, 4·3%), $\lambda_{max.}$ 260, 360 (broad) mμ (log ε 4·65, 3·76), $\nu_{max.}$ (in CCl_4) 1770, 1680 cm.$^{-1}$.

Oxidation of this product (10 mg.) with chromium trioxide (30 mg.) in acetic acid (1 c.c.) afforded naphtho[2,3-*b*]thiophen-4,9-quinone, m. p. and mixed m. p. 226—228°.

Dimethyl sulphate (2 c.c.) was gradually added to a boiling solution of the acetoxy-acetyl compound (170 mg.) in 20% sodium hydroxide (3 c.c.) under nitrogen. The solution was boiled for 12 hr., and kept alkaline by periodic addition of sodium hydroxide. The neutral product (119 mg.) was filtered through alumina, and afforded 9-*acetyl*-4-*methoxynaphtho*[2,3-b]*thiophen* as pale yellow blades, m. p. 118—119° (from cyclohexane) (Found: C, 70·2; H, 4·8. $C_{15}H_{12}O_2S$ requires C, 70·3, H, 4·7%), $\lambda_{max.}$ 262, (267), 350—400 mμ (log ε 4·63, 4·57, 3·62—3·49) $\nu_{max.}$ (in $CHCl_3$) 1670 cm.$^{-1}$.

[7] Dannenberg and Dannenberg-von Dressler, *Annalen*, 1954, **585**, 1; 1955, **593**, 232.

Naphtho[2,3-b]*thiophen.*—(*a*) The 4-acetoxy-compound (1 g.) was boiled for 6 hr. with a solution of tricyclohexyloxyaluminium prepared from aluminium (2 g.) and cyclohexanol (60 c.c.).[4] Cyclohexanol was distilled off rapidly with steam, and the residue extracted with benzene. The crude product was filtered through alumina in benzene–light petroleum (b. p. 60—80°) (1 : 1) and naphtho[2,3-*b*]thiophen (700 mg.) was obtained as plates, m. p. 192—193° (from ethanol–benzene) undepressed when mixed with an authentic specimen prepared by reduction of the quinone.[1]

Desulphurisation of the compound (50 mg.) with Raney nickel (3 g.) in boiling ethanol (20 c.c.) for 12 hr. afforded 2-ethylnaphthalene, identified as the picrate, m. p. and mixed m. p. 75—76°.

(*b*) A solution of the acetoxy-compound (250 mg.) in 10% sodium hydroxide (10 c.c.) and toluene (1 c.c.) was boiled with zinc dust (1·5 g.) under nitrogen for 24 hr. The alkaline solution was extracted with benzene, and the crude product (140 mg.) filtered through alumina in benzene solution. Naphtho[2,3-*b*]thiophen (120 mg.) was obtained as plates (from ethanol–benzene), m. p. and mixed m. p. 192—193°.

2,3-*Dihydrobenzo*[b]*thiophen.*—A solution of thioindoxyl (50 g.), potassium hydroxide (46 g.), and 90% hydrazine hydrate (70 c.c.) in diethylene glycol (350 c.c.) was boiled for 3 hr. under nitrogen. The temperature was slowly raised to 200° and the distillate collected and extracted with benzene, affording 2,3-dihydrobenzo[*b*]thiophen as an oil, b. p. 108—110°/20 mm. (31·5 g.), n^{19}_{D} 1·6092 (Found: C, 70·6; H, 6·2. Calc. for C_8H_8S: C, 70·6; H, 5·9%). The sulphone formed plates, m. p. 88—89° (Found: C, 57·1; H, 4·7. Calc. for $C_8H_8O_2S$: C, 57·1; H, 4·8%). Bennett and Hafez [8] record m. p. 98° for the sulphone. Dehydrogenation with sulphur at 250—260° afforded benzo[*b*]thiophen, m. p. 30° (picrate m. p. 147—148°).

Condensation of 2,3-*Dihydrobenzo*[b]*thiophen with Succinic Anhydride.*—A solution of succinic anhydride (13·9 g.) and aluminium chloride (37 g.) in nitrobenzene (300 c.c.) was added to 2,3-dihydrobenzo[*b*]thiophen (17 g.) in nitrobenzene (100 c.c.) at 0°. After 2 hr. at room temperature ice and hydrochloric acid were added and nitrobenzene was removed in steam. The recovered *oxo-acid* (11·6 g.) crystallised from methyl acetate as prisms, m. p. 151—154° (Found: C, 61·2; H, 5·1. $C_{12}H_{12}O_3S$ requires C, 61·0; H, 5·1%). The *methyl ester*, prepared with diazomethane, formed plates, m. p. 71—72° (from cyclohexane) (Found: C, 62·4; H, 5·4. $C_{13}H_{14}O_3S$ requires C, 62·4; H, 5·7%).

γ-(2,3-*Dihydro*-5-*benzo*[b]*thienyl*)*butyric Acid.*—A solution of the foregoing acid (5·3 g.), sodium hydroxide (4 g.), and 90% hydrazine hydrate (6 c.c.) in diethylene glycol (60 c.c.) was boiled for 1 hr. under nitrogen. Heating was then continued for 4 hr. at 200°. The cooled solution was diluted with water, acidified, and extracted with benzene. The *butyric acid* crystallised from cyclohexane as blades (2·8 g.), m. p. 99—100° (Found: C, 65·0; H, 6·2. $C_{12}H_{14}O_2S$ requires C, 64·8; H, 6·4%).

This acid (250 mg.) was desulphurised with Raney nickel (3 g.) in boiling sodium hydroxide solution for 6 hr. The recovered gum (120 mg.) and 30% nitric acid (5 c.c.) were heated at 180—190° for 30 hr. and the product was esterified with diazomethane. Crystallisation from methanol afforded dimethyl isophthalate as needles, m. p. and mixed m. p. 60°.

2,3,5,6,7,8-*Hexahydro*-8-*oxonaphtho*[2,3-b]*thiophen.*—A solution of the above acid (10 g.) in hydrofluoric acid (200 c.c.) was kept at room temperature for 2 days. The recovered neutral product was filtered through alumina and the *ketone* was obtained as needles (7·9 g.), m. p. 88—89° (from cyclohexane) (Found: C, 70·4; H, 6·2. $C_{12}H_{12}OS$ requires C, 70·5; H, 5·9%).

Reduction of this ketone (1·0 g.) with 90% hydrazine hydrate (2 c.c.) and potassium hydroxide (0·9 g.) in diethylene glycol (20 c.c.) at 145° for 1 hr. and then at 180° for 4 hr., and chromatography of the crude product on alumina, afforded 2,3,5,6,7,8-*hexahydronaphtho*[2,3-b]-*thiophen* (655 mg.) as plates, m. p. 37—38·5° (from benzene–methanol) (Found: C, 75·5; H, 7·4. $C_{12}H_{14}S$ requires C, 75·7; H, 7·4%).

2,3,5,6-*Tetrahydronaphtho*[2,3-b]*thiophen*-8-*ol.*—The hexahydro-ketone (10·0 g.) was reduced with sodium borohydride (1·2 g.) in dioxan–methanol (200 c.c.) overnight. The *carbinol* crystallised from benzene–light petroleum as needles (9·4 g.), m. p. 97—99° (Found: C, 70·7; H, 6·6. $C_{12}H_{14}OS$ requires C, 71·2; H, 7·1%).

Dehydration of this material (9·4 g.) with potassium hydrogen sulphate (2·4 g.) at 150—160° for 20 min., and purification of the product by chromatography on alumina, afforded the *tetrahydro-compound* (5·4 g.) as plates, m. p. 70—71° (from benzene–methanol) (Found: C, 76·5; H, 6·4. $C_{12}H_{12}S$ requires C, 76·5; H, 6·4%); $\lambda_{max.}$ 246, (274), 320 mμ [log ε 4·56, (3·70), 3·44].

[8] Bennett and Hafez, *J.*, 1941, 287.

Dehydrogenation.—The hexahydro-compound described above (4·8 g.) and sulphur (2·4 g.) were heated at 240° for 2 hr. The crude product (3·0 g.) was chromatographed on alumina. Elution with light petroleum (b. p. 40—60°) afforded crystals, m. p. 49—51°; $\lambda_{max.}$ 234, 265, 294, 299, 305 mμ (log $E^{1\%}_{1\,cm.}$ 3·19, 2·50, 1·89, 1·74, 1·91) was similar to that of benzo[*b*]thiophen, suggesting that this product may be 5,6,7,8-tetrahydronaphtho[2,3-*b*]thiophen. It was not further investigated. Continued elution with light petroleum containing increasing proportions of benzene then gave naphtho[2,3-*b*]thiophen (280 mg.), m. p. and mixed m. p. 192°. Later eluates afforded further crops (about 2 g.) of naphtho[2,3-*b*]thiophen, but the ultraviolet absorption spectra, with inflections at 286 and 298 mμ, indicated that these fractions were contaminated with small amounts of the dihydro-compound described below. Pure material was obtained by further chromatography on alumina, and elution with light petroleum (b. p. 60—80°) containing increasing proportions of ether.

A similar impure product was obtained by dehydrogenation of the tetrahydro-compound with sulphur, or with chloranil in boiling xylene. The impurity was difficult to separate by chromatography and was best obtained by removal of the naphtho[2,3-*b*]thiophen from the mixture by reaction with maleic anhydride.[9] 2,3-*Dihydronaphtho*[2,3-b]*thiophen* was then obtained as plates, m. p. 149—151° (Found: C, 77·4; H, 5·3%; *M*, 184. $C_{12}H_{10}S$ requires C, 77·4; H, 5·4%; *M*, 186); $\lambda_{max.}$ 219, (250), 257; 276, 286, 297; 330, 336, 343 mμ [log ε 4·37, (4·42), 4·46; 3·86, 3·93, 3·78; 3·43, 3·42, 3·45]. This spectrum was very similar to that of methyl 2-naphthyl sulphide which had $\lambda_{max.}$ 252, 272, 282 (292), 324, 339 mμ [log ε 4·50, 3·85, 3·93, (3·82), 3·09, 3·06]. The substance (100 mg.) with sulphur (18 mg.) in a sealed tube at 250° for 1·5 hr. gave pure naphtho[2,3-*b*]thiophen (73 mg.), identified by mixed m. p. and ultraviolet absorption.

Cyclisation of γ-(2,3-Dihydro-5-benzo[b]*thienyl)butyric Acid with Stannic Chloride.*—The acid (350 mg.) and phosphorus pentachloride (350 mg.) in benzene (5 c.c.) were kept at room temperature for 1 hr. A solution of stannic chloride (1 c.c.) in benzene (4 c.c.) was added, and the neutral product (250 mg.) distilled at 110°/0·2 mm. (air bath) (Found: C, 70·5; H, 5·6. Calc. for $C_{12}H_{12}OS$: C, 70·5; H, 5·9%). Reduction of this material with lithium aluminium hydride in ether, and heating the product with sulphur at 190° for 2 hr., afforded a mixture which was chromatographed on alumina. Elution with light petroleum containing increasing proportions of benzene afforded a fraction from which naphtho[2,1-*b*]thiophen was obtained by crystallisation; it had m. p. 110° not depressed when mixed with authentic material. Further elution afforded naphtho[2,3-*b*]thiophen, m. p. and mixed m. p. 189° (from ethanol).

γ-(5-Benzo[b]*thienyl)butyric Acid.*—Methyl γ-(2,3-dihydro-5-benzo[*b*]thienyl)butyrate (1 g.) was heated with sulphur (165 mg.) at 220—240° for 1 hr. The product was distilled at 130—140°/0·2 mm. (air bath) and the distillate boiled with aqueous alcoholic potassium hydroxide. The *butyric acid* was obtained as plates (0·39 g.), m. p. 82—83° (from cyclohexane) (Found: C, 65·5; H, 5·6. $C_{12}H_{12}O_2S$ requires C, 65·4; H, 5·5%), $\lambda_{max.}$ 230, 250—260, (265), 285, 290—295, 302 mμ [log ε 4·57, 3·86, (3·75), 3·22, 3·34, 3·48]. The mother liquors furnished a further crop (0·33 g.), m. p. 79—82°.

Cyclisation of γ-(5-Benzo[b]*thienyl)butyric Acid.*—The acid (500 mg.) in benzene (10 c.c.) was treated with phosphorus pentachloride (525 mg.) at room temperature for 3 hr. A solution of stannic chloride (1·25 g.) in benzene (10 c.c.) was added at 0°. The red solution was kept at room temperature for 45 min., ice and hydrochloric acid were added, and the crude product (460 mg.) was chromatographed on alumina. Elution with benzene afforded 4,5,6,7-*tetrahydro*-4-*oxonaphtho*[2,1-b]*thiophen* (238 mg.) as needles, m. p. 54—55° (from light petroleum) (Found: C, 71·2; H, 5·0. $C_{12}H_{10}OS$ requires C, 71·3; H, 5·2%), $\lambda_{max.}$ 225, 251, 320 mμ (log ε 4·28 4·53; 4·11). Further elution gave 5,6,7,8-*tetrahydro*-8-*oxonaphtho*[2,3-b]*thiophen* (30 mg.) as rhombs, m. p. 114—118° (from light petroleum) (Found: C, 71·3; H, 5·2%); $\lambda_{max.}$ 219, (230), 249; 296; 339 mμ [log ε 4·26, (4·24), 4·36, 4·21, 3·70].

Reduction of the ketone (230 mg.), m. p. 54—55°, with lithium aluminium hydride (200 mg.) in boiling ether and dehydration of the resulting carbinol with potassium hydrogen sulphate (50 mg.) at 150—160° for 15 min. afforded an oil (160 mg.) which was distilled at 100—120°/0·2 mm. (air bath) and dehydrogenated with sulphur (30 mg.) at 220—240° for 1 hr. Chromatography on alumina afforded naphtho[2,1-*b*]thiophen (116 mg.) as plates, m. p. and mixed m. p. 113—114°, $\lambda_{max.}$ (230), 243, (251), (280), 291, 302, (314), 330 mμ (log ε 4·45, 4·64, 4·37, 3·89,

[9] Carruthers, future communication.

4·06, 4·01, 3·26, 3·10). The picrate formed orange-red needles, m. p. 146—148° (lit.[10] 146—147°).

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[10] Carruthers, *J.*, 1953, 4186.