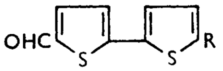
656. *Thiophen Derivatives. Part XIV.*[1] *Some Problems of Substitution in the 2,2'-Bithienyl Series.*

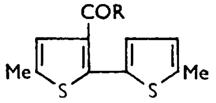
By E. Lescot, jun., Ng. Ph. Buu-Hoï, and N. D. Xuong.

2,2'-Bithienyl is shown to undergo formylation in the 5-position, 5-methyl-2,2'-bithienyl in the 5'-position, and 5,5'-dimethyl-2,2'-bithienyl in the 3-position. 5-(2-Thienylmethyl)-2,2'-bithienyl is formylated in the 5'-position. Numerous new derivatives of 2,2'-bithienyl have been prepared.

The reactivity of 2,2'-bithienyl has scarcely been investigated. This compound has now been found to react vigorously with dimethylformamide in the presence of phosphorus oxychloride, to give 5-formyl-2,2'-bithienyl (I; R = H); 5-methyl-2,2'-bithienyl, obtained by Wolff–Kishner reduction of this aldehyde, similarly underwent formylation to 5-formyl-5'-methyl-2,2'-bithienyl (I; R = Me). The orientation in both aldehydes was deduced from the fact that reduction of the latter afforded 5,5'-dimethyl-2,2'-bithienyl, which had already been prepared by an Ullmann reaction with 2-iodo-5-methylthiophen.[2] In the case of 5,5'-dimethyl-2,2'-bithienyl, formylation occurred in the 3-position, since the resulting aldehyde (II; R = H) was oxidised to an acid identical with that obtained by hypobromite oxidation of 3-acetyl-5,5'-dimethyl-2,2'-bithienyl (II; R = Me); this ketone constituted a by-product in the preparation of the already known 3,3'-diacetyl-5,5'-dimethyl-2,2'-bithienyl.[3] Hypobromite oxidation of the diketone gave 5,5'-dimethyl-2,2'-bithienyl-3,3'-dicarboxylic acid, which readily afforded αα'-dipropyladipic acid on hydrogenolysis with Raney nickel.

(I)





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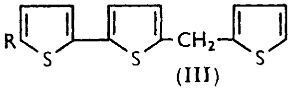

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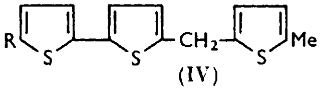

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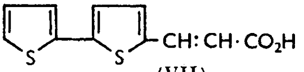
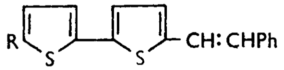
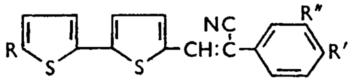


(VII)

(V)





(VI)

An interesting problem of orientation in the same series is offered by formylation of 5-(2-thienylmethyl)-2,2'-bithienyl (III; R = H) [prepared by reduction of 5-(2-thenoyl)-2,2'-bithienyl], experiment showing that the formyl group enters the 5'-position; the aldehyde (III; R = CHO) gave on Wolff–Kishner reduction a compound (III; R = Me) which was different from 5-(5-methyl-2-thienylmethyl)-2,2'-bithienyl (IV), prepared by reduction of 5-(5-methyl-2-thenoyl)-2,2'-bithienyl. These results point to the very high reactivity of the positions 5 and 5' in the molecule of bithienyl, surpassing even that of the position 5 in a 2-alkylthiophen.

The aldehydes in the 2,2'-bithienyl series were yellow, owing to the high degree of conjugation, but otherwise displayed the general reactive features of aromatic aldehydes; 5-formyl- and 5-formyl-5'-methyl-2,2'-bithienyl, for instance, with benzylmagnesium chloride gave alcohols, which were dehydrated to 5-styryl- (V; R = H) and 5-methyl-5'-styryl-2,2'-bithienyl (V; R = Me) respectively. Like the aldehydes, these highly conjugated molecules were pale yellow. More intensely coloured were the acrylonitriles

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[1] Part XIII, Lamy, Lavit, and Buu-Hoï, *J.*, 1958, 4202.

[2] Steinkopf, Leitsmann, Müller, and Wilhelm, *Annalen*, 1939, **541**, 271.

[3] Steinkopf and von Petersdorff, *Annalen*, 1940, **543**, 123.

(VI) prepared by alkali-catalysed condensation of the aldehydes with arylacetonitriles;[4] so also were the chalcones derived by condensation with thiophen ketones. 5-Formyl-2,2′-bithienyl condensed readily with ethyl hydrogen malonate, to give the ethyl ester of the yellow β-(2,2′-bithienyl-5-yl)acrylic acid (VII).

EXPERIMENTAL

5-*Formyl*-2,2′-*bithienyl* (I; R = H).—2,2′-Bithienyl (b. p. 129—131°/15 mm.; m. p. 34°) was obtained[5] from 2-iodothiophen and copper powder, along with 2,2′,2″-terthienyl (b. p. 204—210°/0·5 mm.; m. p. 95°) and 2,2′,2″,2‴-quaterthienyl (b. p. 290—315°/0·6 mm.; m. p. 210°). To a mixture of 2,2′-bithienyl (20 g.), dimethylformamide (13·5 g.), and dry toluene (100 c.c.), phosphorus oxychloride (27·6 g.) was added in small portions with stirring, giving rise to an exothermic reaction; after the reaction had subsided, the mixture was heated for 5 hr. on a water-bath and, after cooling, shaken with warm saturated aqueous sodium acetate (200 c.c.). The organic layer was taken up in toluene, the toluene solution was washed with water, dilute aqueous sodium carbonate, and again water, dried (Na_2SO_4), and evaporated under reduced pressure, and the residue was fractionated *in vacuo*. The *aldehyde* (17 g.), b. p. 210°/18 mm., formed pale leaflets, m. p. 59°, from ethanol (Found: C, 55·4; H, 3·0. $C_9H_6OS_2$ requires C, 55·6; H, 3·0%). The *thiosemicarbazone* formed yellow prisms, m. p. 197°, from ethanol (Found: C, 45·0; H, 3·4. $C_{10}H_9N_3S_3$ requires C, 44·7; H, 3·3%); the 4-*oxo*-Δ^2-*thiazolin*-2-*ylhydrazone* formed yellow prisms, m. p. 269°, from ethanol (Found: C, 46·9; H, 3·0. $C_{12}H_9ON_3S_3$ requires C, 46·7; H, 3·1%). Reduction of this aldehyde with hydrazine hydrate and potassium hydroxide in diethylene glycol[6] gave an 80% yield of 5-methyl-2,2′-bithienyl.[7]

β-(2,2′-*Bithienyl*-5-*yl*)*acrylic Acid* (VII).—A solution of the foregoing aldehyde (5 g.) and ethylhydrogen malonate (6 g.) in anhydrous pyridine (50 c.c.) was treated with piperidine (1 c.c.), left for 72 hr., then heated for 1 hr. on a water-bath; most of the pyridine was distilled off *in vacuo*, and water was added to the residue. The product was taken up in ether, and the ethereal solution washed with dilute hydrochloric acid, then with water, dried (Na_2SO_4), and evaporated. The *ethyl ester* (5 g.), b. p. 240°/16 mm., formed pale yellow needles, m. p. 66° (Found: C, 58·9; H, 4·5. $C_{13}H_{12}O_2S_2$ requires C, 59·1; H, 4·6%). The free *acid* obtained on saponification formed yellow prisms, m. p. 177°, from aqueous acetic acid (Found: C, 55·7; H, 3·5. $C_{11}H_8O_2S_2$ requires C, 55·9; H, 3·3%).

5-*Styryl*-2,2′-*bithienyl* (V; R = H).—To a Grignard reagent prepared from benzyl chloride (3·6 g.) and magnesium (0·7 g.) in ether (75 c.c.), 5-formyl-2,2′-bithienyl (3 g., in benzene) was added in small portions, and the reaction completed by 15 minutes' heating on a water-bath. After decomposition with cold dilute aqueous sulphuric acid, the ethereal layer was washed with water and dried (Na_2SO_4), and the crude alcohol obtained on evaporation was dehydrated by hot formic acid (5 g.). After cooling and dilution with water, the product was taken up in benzene, washed with water and dried (Na_2SO_4), recovered, and fractionated *in vacuo*. The portion of b. p. 220—240°/0·3 mm. (3 g.) crystallised as yellow needles, m. p. 115° from methanol (Found: C, 71·3; H, 4·4. $C_{16}H_{12}S_2$ requires C, 71·6; H, 4·5%).

5-*Formyl*-5′-*methyl*-2,2′-*bithienyl* (I; R = Me).—Prepared from 5-methyl-2,2′-bithienyl (10 g.), dimethylformamide (7 g.), and phosphorus oxychloride (19 g.) in toluene, this *aldehyde* (9·5 g.), b. p. 208°/18 mm., formed pale yellow prisms, m. p. 98°, from ethanol (Found: C, 57·7; H, 3·8. $C_{10}H_8OS_2$ requires C, 57·6; H, 3·8%). Wolff–Kishner reduction afforded an 80—85% yield of 5,5′-dimethyl-2,2′-bithienyl, m. p. 68° (lit.,[2] m. p. 67°).

5-*Methyl*-5′-*styryl*-2,2′-*bithienyl* (V; R = Me).—Prepared from the appropriate aldehyde (4 g.) and benzylmagnesium chloride, this *compound* (2·5 g.) formed yellow prisms, m. p. 125—126°, from methanol (Found: C, 72·3; H, 5·1. $C_{17}H_{14}S_2$ requires C, 72·3; H, 5·0%).

3-*Formyl*-5,5′-*dimethyl*-2,2′-*bithienyl* (II; R = H).—Obtained from 5,5′-dimethyl-2,2′-bithienyl (8 g.), dimethylformamide (5 g.), and phosphorus oxychloride (7 g.) in toluene, this *compound* (7·5 g.) crystallised as pale yellow leaflets, m. p. 65°, from ethanol (Found: C, 59·8; H, 4·8. $C_{11}H_{10}OS_2$ requires C, 59·5; H, 4·5%).

3-*Acetyl*-5,5′-*dimethyl*-2,2′-*bithienyl* (II; R = Me).—To a solution of 5,5′-dimethyl-2,2′-bithienyl (15 g.) and acetyl chloride (7 g.) in carbon disulphide (75 c.c.), stannic chloride (33·5 g.)

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[4] Cf. Buu-Hoï, Hoán, and Lavit, *J.*, 1950, 2130; 1952, 4590.

[5] Cf. Eberhard, *Ber.*, 1894, **27**, 2919; Steinkopf and Roch, *Annalen*, 1930, **482**, 260.

[6] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.

[7] Steinkopf, Leitsmann, and Hofmann, *Annalen*, 1941, **546**, 180.

was added in small portions with stirring, and the mixture left for 2 hr. at room temperature, then poured into cold dilute hydrochloric acid; the organic layer was washed with dilute aqueous sodium hydroxide, then with water, dried (Na_2SO_4), the solvent was removed, and the residue fractionated *in vacuo*. The *ketone* (8 g.) formed a pale yellow oil, n_D^{26} 1·6652, which solidified to a crystalline mass, m. p. 49° after recrystallisation from light petroleum (Found: C, 60·7; H, 4·9. $C_{12}H_{12}OS_2$ requires C, 61·0; H, 5·1%). The higher-boiling portion gave, on recrystallisation from ethanol, 3,3′-diacetyl-5,5′-dimethyl-2,2′-bithienyl (3 g.), m. p. 111° (lit.,[3] 111°).

5,5′-*Dimethyl*-2,2′-*bithienyl*-3-*carboxylic Acid*.—To a suspension of 3-formyl-5,5′-dimethyl-2,2′-bithienyl (5 g.) in 1% aqueous sodium hydroxide, a 4% aqueous solution of potassium permanganate (2·3 g.) was added dropwise with stirring, at 5—10°; after 1 hour's stirring, a few drops of sodium hydrogen sulphite were added, the precipitate of manganese oxide was filtered off, and the filtrate acidified with hydrochloric acid. The *acid* which was precipitated formed pale yellow needles (2·5 g.), m. p. 151°, from aqueous acetic acid (Found: C, 55·4; H, 4·2. $C_{11}H_{10}O_2S_2$ requires C, 55·4; H, 4·1%). This acid was identical with the product of oxidation of 3-acetyl-5,5′-dimethyl-2,2′-bithienyl with sodium hypobromite in aqueous dioxan.

5,5′-*Dimethyl*-2,2′-*bithienyl*-3,3′-*dicarboxylic Acid*.—Finely powdered 3,3′-diacetyl-5,5′-dimethyl-2,2′-bithienyl (3 g.) was shaken for 3 hr. with an aqueous solution (50 c.c.) of sodium hypobromite prepared from bromine (2·3 c.c.) and sodium hydroxide (4·1 g.); the bromoform was decanted off, and the aqueous layer treated with sodium hydrogen sulphite and acidified with hydrochloric acid. The *diacid* which was precipitated formed yellowish prisms (2 g.), m. p. 296—298°, from aqueous acetic acid (Found: C, 50·7; H, 3·7. $C_{12}H_{10}O_4S_2$ requires C, 51·0; H, 3·5%).

αα-*Dipropyladipic Acid*.[8]—To a solution of the above diacid (3 g.) in 10% aqueous sodium hydroxide (300 c.c.), Raney nickel (60 g.) was added portionwise with stirring, stirring was continued, and the mixture heated on a water-bath for 2 hr. The precipitated nickel was filtered off and washed with water, and the cooled filtrate was acidified with hydrochloric acid. The organic *acid* was taken up in ether, washed with water, and dried (Na_2SO_4); the residue left on evaporation of the solvent formed colourless prisms, m. p. 100—101°, from light petroleum (Found: C, 58·3; H, 9·5. $C_{12}H_{22}O_4,H_2O$ requires C, 58·0; H, 9·6%).

5-(2-*Thenoyl*)-2,2′-*bithienyl*.—To a solution of 2,2′-bithienyl (12 g.) and 2-thenoyl chloride (13·2 g.) in carbon disulphide (75 c.c.), stannic chloride (32·5 g.) was added portionwise with stirring, and the mixture left for 2 hr. at room temperature, then worked up in the usual way. The *ketone* (10 g.), b. p. 265—270°/18 mm., formed yellow needles, m. p. 104° (from ethanol) (Found: C, 56·7; H, 3·0. $C_{13}H_8OS_3$ requires C, 56·5; H, 2·9%).

5-(2-*Thienylmethyl*)-2,2′-*bithienyl* (III; R = H).—A solution of the foregoing compound (5 g.) and 95% hydrazine hydrate (5 g.) in diethylene glycol (30 c.c.) was briefly refluxed to allow the hydrazone to form, and, after cooling, potassium hydroxide (5 g.) was added; the mixture was then refluxed for 2 hr. with removal of water and, when cool, acidified with dilute hydrochloric acid. The *product* was taken up in benzene, washed with water, dried ($CaCl_2$), recovered, and fractionated *in vacuo*. The portion (3·5 g.), b. p. 225—228°/15 mm., n_D^{27} 1·6991, formed colourless needles, m. p. 46°, from ethanol (Found: C, 59·7; H, 4·1. $C_{13}H_{10}S_3$ requires C, 59·5; H, 3·8%).

5-*Formyl*-5′-(2-*thienylmethyl*)-2,2′-*bithienyl* (III; R = CHO).—Prepared in the usual way from the foregoing compound (6 g.), dimethylformamide (2·5 g.), and phosphorus oxychloride (5·3 g.) in toluene (50 c.c.), this *aldehyde* (5·2 g.), b. p. 265—268°/17 mm., formed yellow prisms, m. p. 109°, from ethanol (Found: C, 57·9; H, 3·5. $C_{14}H_{10}OS_3$ requires C, 57·9; H, 3·5%).

5-*Methyl*-5′-(2-*thienylmethyl*)-2,2′-*bithienyl* (III; R = Me).—Prepared by reduction of the preceding aldehyde (1·7 g.) with hydrazine hydrate (1·7 g.) and potassium hydroxide (1·7 g.) in diethylene glycol (15 c.c.), this *compound* (1 g.) crystallised as colourless leaflets, m. p. 42°, from light petroleum (Found: C, 60·8; H, 4·2. $C_{14}H_{12}S_3$ requires C, 60·9; H, 4·4%).

5-(5-*Methyl*-2-*thenoyl*)-2,2′-*bithienyl*.—Prepared from 2,2′-bithienyl (8 g.), 5-methyl-2-thenoyl chloride (8 g.), and stannic chloride (25 g.) in carbon disulphide, this *ketone* (7 g.), b. p. 289—290°/18 mm., formed yellow needles, m. p. 103°, from ethanol (Found: C, 57·8; H, 3·4. $C_{14}H_{10}OS_3$ requires C, 57·9; H, 3·5%).

5-(5-*Methyl*-2-*thienylmethyl*)-2,2′-*bithienyl* (IV; R = H).—Obtained by reduction of the

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[8] For similar hydrogenolysis of thiophen compounds to aliphatic diacids, see Buu-Hoï, Sy, and Xuong, *Compt. rend.*, 1955, **240**, 442.

foregoing compound (2·5 g.) with hydrazine hydrate (2·5 g.) and potassium hydroxide (2·5 g.) in diethylene glycol (15 c.c.), this *compound* (2 g.), b. p. 243—245°/15 mm., n_D^{25} 1·6857, formed colourless leaflets, m. p. 44°, from light petroleum (Found: C, 60·8; H, 4·3%).

β-(2,2′-*Bithienyl*-5-*yl*)-α-*phenylacrylonitrile* (VI; R = R′ = R″ = H).—To a solution of 5-formyl-2,2′-bithienyl (0·2 g.) and phenylacetonitrile (0·2 g.) in ethanol, a few drops of 25% aqueous sodium hydroxide were added with stirring, producing immediately a precipitate of the *nitrile*, which was collected, washed with water, and recrystallised from acetone as orange-yellow leaflets (2 g.), m. p. 147°, giving a red halochromy in sulphuric acid (Found: C, 69·7; H, 3·5. $C_{17}H_{11}NS_2$ requires C, 69·6; H, 3·8%).

α-p-*Chlorophenyl*-β-(2,2′-*bithienyl*-5-*yl*)*acrylonitrile* (VI; R = R″ = H; R′ = Cl), prepared from *p*-chlorophenylacetonitrile, formed orange-yellow leaflets, m. p. 204° (from acetone) (Found: C, 62·6; H, 3·2. $C_{17}H_{10}NS_2Cl$ requires C, 62·3; H, 3·1%); β-(2,2′-*bithienyl*-5-*yl*)-α-(3,4-*dichlorophenyl*)*acrylonitrile* (VI; R = H; R′ = R″ = Cl) formed orange-yellow needles, m. p. 223° (from acetone) (Found: C, 56·5; H, 2·5. $C_{17}H_9NS_2Cl_2$ requires C, 56·4; H, 2·5%); α-p-*chlorophenyl*-β-(5′-*methyl*-2,2′-*bithienyl*-5-*yl*)*acrylonitrile* (VI; R = Me; R′ = Cl; R″ = H), similarly prepared from the aldehyde (I; R = Me), formed orange leaflets, m. p. 189°, from acetone, giving a violet halochromy in sulphuric acid (Found: C, 63·0; H, 3·6. $C_{18}H_{12}NS_2Cl$ requires C, 63·3; H, 3·5%).

α-(2,2′-*Bithienyl*-5-*yl*)-β-(5-*chloro*-2-*thenoyl*)*ethylene*.—Prepared by shaking a solution of 5-formyl-2,2′-bithienyl (0·2 g.) and 2-acetyl-5-chlorothiophen (0·2 g.) in ethanol with a few drops of 20% aqueous sodium hydroxide, this *ketone* formed deep yellow needles, m. p. 120°, from ethanol, giving a brown-red halochromy in sulphuric acid (Found: C, 53·7; H, 2·9. $C_{15}H_9OS_3Cl$ requires C, 53·5; H, 2·7%); β-(5-*chloro*-2-*thenoyl*)-α-(5,5′-*dimethyl*-2,2′-*bithienyl*-3-*yl*)*ethylene*, similarly prepared from the aldehyde (II; R = H), formed deep yellow needles, m. p. 136° (from ethanol), giving a violet halochromy in sulphuric acid (Found: C, 55·6; H, 3·7. $C_{17}H_{13}OS_3Cl$ requires C, 55·9; H, 3·6%).

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