1310. *Naturally-occurring Thiophens. Bithienyl Derivatives from* Tagetes minuta *L.*

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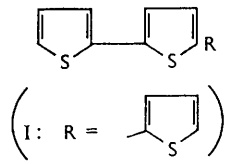
The roots of *Tagetes minuta* L. contain various 5-(R-substituted)-2,2′-bithienyls, *e.g.*, (I; R = α-thienyl), (II; R = C:C·CH:CH$_2$), (IX; R = C:C·CH$_2$·CH$_2$·OH), and (X; R = C:C·CHOH·CH$_2$Cl). Syntheses of (II), (IX), the *cis*-isomer of the derivative (XIII; R = CH:CH·CH$_2$·CH$_2$·OH), and various investigations relating to the derivative (VI; R = C:CH) are described.

Naturally occurring thiophens are now a well established group of natural products, and recent reviews [1-3] included summaries of the types which have been described. As part of a general study, the thiophen derivatives present in the roots of *Tagetes minuta* L. (syn. *T. glandulifera* Schrank) have been investigated, and some of our results have been published in a preliminary Communication.[4]

Other Tagetes species, *e.g.*, *T. erecta* and *T. patula*, have been shown [5] to possess nematicidal activity, and Uhlenbroek and Bijloo [6,7] isolated from the roots of these species two thiophen derivatives which appeared to be responsible for at least part of this activity. These were α-terthienyl (I), which had previously been isolated from the flowers of *Tagetes erecta*,[8] and 5-(but-3-en-1-ynyl)-2,2′-bithienyl (II), the structure of which was based on degradative and spectral evidence. The latter was criticised by Sörensen [9] who suggested that the structure of the compound was probably (III).

[1] F. Bohlmann, *Chimia (Switz.)*, 1962, **16**, 353.
[2] F. Bohlmann, H. Bornowski, and C. Arndt, *Fortschr. Chem. Forsch.*, 1962, **4**, 138.
[3] F. Bohlmann, *Planta Medica*, 1964, **12**, 384.
[4] R. E. Atkinson, R. F. Curtis, and G. T. Phillips, *Tetrahedron Letters*, 1964, 3159.
[5] A. F. G. Slootweg, *Nematologica*, 1956, **1**, 192.
[6] J. H. Uhlenbroek and J. D. Bijloo, *Rec. Trav. chim.*, 1959, **78**, 382.
[7] J. H. Uhlenbroek and J. D. Bijloo, *Rec. Trav. chim.*, 1958, **77**, 1004.
[8] J. W. Sease and L. Zechmeister, *J. Amer. Chem. Soc.*, 1947, **69**, 273.
[9] N. A. Sörensen, *Proc. Chem. Soc.*, 1961, 98.

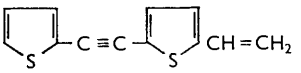
Tagetes minuta L. is a common weed in Southern Rhodesia. The plant possesses significant nematicidal activity[10] against *Meloidogyne javanica*, the tobacco-root eelworm, which is a serious pest in some tobacco areas, so we examined the roots for the presence of thiophen derivatives which might account for this activity. Comparisons of the root extracts of various *Tagetes* sp. by thin-layer chromatography[11] showed that there was little variation in the qualitative pattern of the spots attributed to thiophen derivatives. Compounds (I) and (II) were the major spots in all the species tested.



(I: R =)

(II: R = C:C·CH:CH$_2$)

(III: R = C:C·CH$_2$·CH:CH$_2$)



(IV)

(V: R = COMe)
(VI: R = C:CH)
(VII: R = C(Cl):CH·CHO)
(VIII: R = C:CBr)
(IX: R = C:C·CH$_2$·CH$_2$·OH)
(X: R = C:C·CHOH·CH$_2$Cl)
(XI: R = CH:CH·CH$_2$·CH$_2$·OAc)
(XII: R = CHO)
(XIII: R = CH:CH·CH$_2$·CH$_2$·OH)
(XIV: R = CCl$_2$·CH$_3$)
(XV: R = CHCl$_2$)

While this work was in progress it became clear that Bohlmann and his co-workers had been pursuing similar objectives with *T. patula* and *T. erecta*,[12] and later with *T. minuta*,[13] but since our approach and results differ in some aspects it is appropriate to record them in detail.

Large scale extracts of the roots of *T. minuta* were purified by chromatography to give α-terthienyl (I) and the second major component as a yellow oil, $C_{12}H_8S_2$. This showed infrared and ultraviolet absorption maxima identical with those recorded by Uhlenbroek and Bijloo[6] for 5-(but-3-en-1-ynyl)-2,2′-bithienyl (II), and a mass spectrum with a highest molecular ion **216**. The nuclear magnetic resonance spectrum, as was pointed out by Bohlmann and Herbst,[12] supported structure (II) but did not preclude structure (IV). A synthesis was desirable.

The two initial steps in our synthesis were identical with those of Bohlmann and Herbst[12] and commenced with 2-acetylbithienyl (V),[14] which was chlorinated with phosphorous pentachloride and dehydrohalogenated by sodamide in liquid ammonia to give 2-ethynylbithienyl (VI). In our hands this reaction gave extremely low yields and similar results have been recorded for thiophen derivatives.[15] One of the major by-products is discussed below.

It was found that a very much more satisfactory route to the acetylene (VI) could be based on a method described by Bodendorf and Kloss[16] for the preparation of 3,4-dimethoxyphenylacetylene. 2-Acetylbithienyl (V) was converted into the corresponding unsaturated chloro-derivative (VII) by treatment with the Vilsmeyer complex from phosphorus oxychloride and dimethylformamide. Direct dehydrohalogenation and decomposition of this chloro-derivative with alkali gave 2-ethynylbithienyl (VI) in very good yield.

2-Ethynylbithienyl (VI) showed atypical properties. While it formed a stable mercury

[10] R. F. Curtis and R. A. C. Daulton, *Nematologica*, 1963, **9**, 357.
[11] R. F. Curtis and G. T. Phillips, *J. Chromatog.*, 1962, **9**, 366.
[12] F. Bohlmann and P. Herbst, *Chem. Ber.*, 1962, **95**, 2945.
[13] F. Bohlmann, K.-M. Kleine, and C. Arndt, *Chem. Ber.*, 1964, **97**, 2125.
[14] M. C. Rebstock and C. D. Stratton, *J. Amer. Chem. Soc.*, 1955, **77**, 3082.
[15] A. Vaitiekunas and F. F. Nord, *J. Org. Chem.*, 1954, **19**, 902.
[16] K. Bodendorf and P. Kloss, *Angew. Chem.*, 1963, **2**, 98.

derivative in the usual way, the corresponding 1-bromo-derivative (VIII) could not be obtained, either by treatment with potassium hypobromite (using conditions under which phenylacetylene readily reacted [17]) or by reaction of the mercury salt with bromine in an inert solvent.[18,19] Attempts to obtain the sodio-derivative by treatment with sodamide in liquid ammonia were also unsuccessful. The ultraviolet absorption spectrum and the infrared spectrum, which showed a terminal acetylenic function, were normal, but the n.m.r. spectrum showed absorption at τ 6·77 which is considerably lower than that normal for acetylenic protons [20] (cf. phenylacetylene, τ 7·07). A shift downfield corresponding to increased deshielding of acetylenic protons has been observed by Cook and Danyluk,[21] and this suggests that the 2,2′-bithienyl residue produces a significant deshielding effect.

The failure to obtain a sodio-derivative of this acetylene precluded direct reaction with ethylene oxide to give the carbinol (IX) but exchange with ethylmagnesium bromide gave a Grignard derivative which could be treated with ethylene oxide under special conditions (see below) to produce the required carbinol. It has been stated [22] that the reaction of acetylenic Grignard derivatives with ethylene oxide gives mainly ethylene bromohydrin, *e.g.*, the reaction of phenylethynylmagnesium bromide with ethylene oxide gave 4-phenylbut-3-yn-1-ol in 20% yield.[23] However, modified techniques,[24,25] involving the removal of the solvent ether and heating the residual Grignard complex, have been claimed to produce the expected β-hydroxyacetylenes. Application of this method in this case gave 5-(4-hydroxybut-1-ynyl)-2,2′-bithienyl (IX) in good yield.

Proof of the structure was complicated by the absence of any absorption in the infrared spectrum which could be assigned to the C:C group. Absence of this absorption is well known in symmetrical molecules [26] but was unexpected in this case. However, the structure was confirmed by the ultraviolet absorption spectrum, which indicated that there was an unsaturated chromophore adjacent to the bithienyl nucleus, and the infrared spectrum, which showed a monosubstituted bithienyl residue and a primary OH group but no absorption in the double-bond region.

By established procedure the acetylenic carbinol (IX) was then converted, through the toluene-*p*-sulphonyl derivative, into 5-(but-3-en-1-ynyl)-2,2′-bithienyl (II), identical with the natural product.

After the isolation of the derivatives (I) and (II), further development of the chromatogram with increasing concentrations of polar solvents gave two fractions containing thiophen derivatives. The major fraction yielded a compound, $C_{12}H_{10}OS_2$, which proved to be identical by direct comparison with the acetylenic carbinol (IX) (see above). The minor fraction gave a very small quantity of a crystalline material, $C_{12}H_9ClOS_2$. We have suggested [4] a tentative structure (X) for this compound. Further investigations will be reported in a later Communication.

No fraction corresponding to *cis*-5-(4-acetoxybut-1-enyl)-2,2′-bithienyl (XI), which Bohlmann and Herbst [12] claimed to have isolated from *T. patula* and *T. erecta*, could be detected in the extracts of *T. minuta*. Since the overall patterns of spots on thin-layer chromatograms produced by the crude extracts from these three species were virtually identical, this was unusual. It appeared to us that the compound (XI) isolated by

[17] R. A. Jacobson and W. H. Carothers, *J. Amer. Chem. Soc.*, 1933, **55**, 4667.
[18] W. H. Carothers, R. A. Jacobson, and G. J. Berchet, *J. Amer. Chem. Soc.*, 1933, **55**, 4665.
[19] G. Eglinton and W. McCrae, *J.*, 1963, 2295.
[20] G. V. D. Tiers, " N.M.R. Summary," Minnesota Mining & Manufacturing Co., St. Paul, Minn., 1961.
[21] C. D. Cook and S. S. Danyluk, *Tetrahedron*, 1963, **19**, 177.
[22] R. A. Raphael, " Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955, p. 18.
[23] J. P. Danehy, R. R. Vogt, and J. A. Nieuwland, *J. Amer. Chem. Soc.*, 1935, **57**, 2327.
[24] M. S. Kharasch and O. Reinmuth, " Grignard Reactions of Non-metallic Compounds," Constable, London, 1954, p. 961.
[25] S. Winstein and R. B. Henderson, " Heterocyclic Compounds," Wiley, New York; Chapman and Hall, London, 1950, vol. 1, p. 55.
[26] L. J. Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 60.

Bohlmann and Herbst [12] might be the acetyl derivative of the acetylenic carbinol (IX). The assignment of the structure (XI) had been based on hydrolysis to the corresponding alcohol (XIII) which contained a conjugated system adjacent to a bithienyl nucleus. In the absence of any absorption due to a C:C bond this was assumed to be a *cis*-double bond (694 cm.$^{-1}$). In our experience the assignment of a *cis*-double bond in a thiophen derivative as a result of absorption at 694 cm.$^{-1}$ is very unreliable; almost all the 5-substituted 2,2′-bithienyl derivatives examined show a peak in this region which is missing from 5,5′-disubstituted derivatives.

Bohlmann and Herbst [12] were unsuccessful in an attempt to synthesise the *cis*-alcohol (XIII) [and through this the acetate (XI)] from 5-formyl-2,2′-bithienyl (XII) and a Wittig reagent derived from the tetrahydropyranyl ether of 3-bromopropan-1-ol; only the *trans*-isomer was obtained. To clarify the position we synthesised the *cis*-alcohol (XIII) from the acetylenic carbinol (IX) by stereospecific reduction either with hydrogen over Lindlar catalyst or by reduction with diborane. Hydrogenation using the technique described by Dobson *et al.*[27] was unsuccessful, but with 1 mole of hydrogen and a large excess of catalyst in ethyl acetate solution, *cis*-5-(4-hydroxybut-1-ynyl)-2,2′-bithienyl (XIII) was easily obtained. This *cis*-isomer showed an appropriate hypsochromic shift (5 mμ) when compared with the *trans*-isomer, and the melting point (57—58°) was clearly different from that of the alcohol (68°) obtained by Bohlmann and Herbst [12] from hydrolysis of the natural acetate. The latter melting point was similar to that of the acetylenic carbinol (IX), and we suggested [4] that the natural product was the acetate derived from this carbinol. Bohlmann and his co-workers [13] have now published further spectral evidence which confirms that the natural product (XI) is the acetate of the carbinol (IX).

An attempt was made to obtain the *cis*-isomer by other methods. Bergel'son and Shemyakin [28] demonstrated that the stereospecific synthesis of *cis*-olefins from alkylidenetriphenylphosphoranes and aldehydes can be achieved in polar solvents such as dimethylformamide in the presence of iodide ions. When the alcohol (XIII) was prepared by the method of Bohlmann and Herbst,[12] but with these modified conditions, only the *trans*-isomer was obtained. Stereospecific reduction of the carbinol (IX) with diborane [29] had limited success; although the *cis*-isomer (XIII) was obtained, the yield was greatly reduced by the formation of extremely insoluble boron complexes.

In an attempt to explain the low yield of 2-ethynylbithienyl (VI) obtained in the dehydrohalogenation sequence, the crude product obtained by the chlorination of 5-acetyl-2,2′-bithienyl (V) was examined. Repeated chromatography in the dark gave two major products one of which was assigned the structure expected from this reaction, 5-(1,1-dichloroethyl)-2,2′-bithienyl (XIV). This compound was extremely unstable but showed an ultraviolet absorption spectrum which was consistent with this structure. The infrared spectrum showed a monosubstituted bithienyl system and C–Cl bond(s) but no absorption in the carbonyl or conjugated double bond region of the spectrum. On treatment with sodamide in liquid ammonia it gave 5-ethynyl-2,2′-bithienyl (VI).

The other product was an unstable solid, m. p. 97—98°. Analysis indicated $C_{8-9}H_6Cl_2S_2$. The mass spectrum showed a highest molecular ion with *m/e* 248, confirming $C_9H_6Cl_2S_2$. The ultraviolet absorption spectrum and the infrared spectrum showed a monosubstituted 2,2′-bithienyl nucleus and C–Cl bonds. This evidence indicated that the compound was 5-dichloromethyl-2,2′-bithienyl (XV) which has a carbon skeleton with one carbon atom less than the starting material. The structure was confirmed by the n.m.r. spectrum which was very simple and showed resonances at only two positions, τ 3·0, equivalent to five protons, and τ 3·33, equivalent to one proton. The latter position is consistent with the heavy deshielding produced by the two chlorine atoms attached to the same carbon

[27] N. A. Dobson, G. Eglinton, M. Krishnamurti, R. A. Raphael, and R. G. Willis, *Tetrahedron*, 1961, **16**, 16.
[28] L. D. Bergel'son and M. M. Shemyakin, *Tetrahedron*, 1963, **19**, 149.
[29] H. C. Brown, *Tetrahedron*, 1961, **12**, 117.

atom as the proton (cf. benzylidene chloride, τ 3·42). The nature of this curious rearrangement is obscure and is the subject of further investigation. It is clearly one of the reasons for the low yield in the dehydrohalogenation sequence to the ethynyl derivative (VI).

There has been some confusion over the nomenclature of *Tagetes minuta* L., and in recent Papers [30,31] it was pointed out that this name was synonymous with *Tagetes glandulifera* Schrank. We are grateful to Sir George Taylor of the Royal Botanic Gardens, Kew, and Dr. J. D. Munro, Tropical Products Institute, London W.C.1, for a definitive statement on the taxonomic situation. " . . . We see no reason to doubt that *Tagetes glandulifera* Schrank is a taxonomic synonym of *T. minuta* L. It was described from a Brazilian specimen, and was reduced to *T. minuta* by J. G. Baker in Martius's Fl. Brasiliensis, vol. vi (pt. 3), p. 273 (1884), also by P. A. Rydberg in ' North American Flora ', vol. 34 (pt. 2), p. 156 (1915). The tradition for giving the name *T. glandulifera* to Australian specimens of the very common American weed *T. minuta* seems to have begun with Bentham, F. Australiensis, vol. iii, 545 (1866), and has evidently died hard. Bentham was following De Candolle who, in his ' Prodromus ', vol. V, p. 644 (1836), unaccountably accepted the name *T. glandulifera* but placed *T. minuta* (which had been described long before) in its synonymy. We know of no-one who has ever attempted to separate the two species on macroscopic grounds." Dr. Munro has further suggested that the differences in composition of the essential oils observed by Dr. G. E. Howard and quoted by Boehm *et al.*[31] were due to variations in distillation technique.

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are corrected. Ultraviolet absorption spectra were measured in ethanol on an Unicam S.P. 800 recording spectrophotometer, and infrared absorption spectra for potassium bromide discs or thin films with Perkin-Elmer 137 or 237 spectrophotometers. N.m.r. spectra were determined in carbon disulphide using tetramethylsilane as an internal standard with a Perkin-Elmer 40 Mc./sec. spectrometer.

Mass spectrometric analyses were carried out by Dr. J. H. Beynon and Mr. A. E. Williams, Imperial Chemical Industries Limited, Dyestuffs Division, Manchester, or Mr. A. R. West and Mr. W. L. Mead, British Petroleum Research Ltd., Sunbury, on MS. 9 mass spectrometers.

Alumina for chromatography was Spence H, acid-washed to neutrality and activated at 110° for 8 hr. B.D.H. Silicagel was used in the inactive form. Thin-layer chromatographic methods have already been described.[11] The following chromatographic systems were used: System A was alumina G (Merck) developed with light petroleum (b. p. 40—60°); system B was silicagel G (Merck) developed with light petroleum (b. p. 40—60°); system C was silicagel G (Merck) developed with benzene–chloroform (5 : 2); system D was alumina G (Merck) developed with n-pentane–acetone (9 : 1); system E was silicagel G–silver nitrate (20%) developed with benzene–chloroform (5 : 3). Colours refer to spray reactions with isatin–sulphuric acid solution.[11]

Isolation Studies on T. minuta *L.*—Fresh roots of *T. minuta* L. (1·8 kg.) were allowed to stand in ether for 4 weeks. The concentrated ether extract (3 g.) was purified by chromatography over alumina (500 g.); elution with n-pentane gave 5-(*but*-3-*en*-1-*ynyl*)-2,2′-*bithienyl* (II) as a pale yellow viscous oil (570 mg.), b. p. 80—100°/0·005 mm., $\lambda_{max.}$ 249, 341 (log ε 3·95, 4·36), $\lambda_{max.}$ (film) 2200 (C:C), 1600, 970, 917 (CH:CH_2), 840 cm.$^{-1}$ (2-thienyl). N.m.r. spectrum: τ 2·9 (5, multiplet, bithienyl protons); 4·2 (3, multiplet, CH:CH_2) [Found: *M* (mass spectrum) 216. Calc. for $C_{12}H_8S_2$: *M*, 216·3], R_F 0·70 (system A, green-black) and 0·52 (system B). Satisfactory analytical data could not be obtained.

Further elution gave 2,2′:5′,2″-terthienyl (I) (460 mg.), plates from n-pentane, m. p. and mixed m. p. 93° (lit.,[32] 94—95·5°) (Found: C, 58·3; H, 3·5. Calc. for $C_{12}H_8S_3$: C, 58·1; H, 3·3%), $\lambda_{max.}$ 252, 350 mμ (log ε 3·96, 4·35), $\nu_{max.}$ 830 (2-thienyl), 800 (thiophen-2,5-diyl), 688 (2-thienyl), R_F 0·57 (system A, red ⟶ blue-green) and 0·54 (system B).

[30] D. H. S. Horn and J. A. Lamberton, *Austral. J. Chem.*, 1963, **16**, 475.
[31] E. E. Boehm, V. Thaller, and M. C. Whiting, *J.*, 1963, 2535.
[32] J. W. Sease and L. Zechmeister, *J. Amer. Chem. Soc.*, 1947, **69**, 270.

Further elution with ether–methanol (9 : 1 v/v) gave an oil containing several components. This was concentrated and the components were separated by chromatography on silica gel (10 × 2 cm.). Elution with n-pentane–ether (3 : 2 v/v) gave a crude fraction which was purified by preparative thin-layer chromatography [system C, but benzene–chloroform (5 : 1)] to give a pale yellow oil (70 mg.). Recrystallisation from n-pentane gave 5-(4-*chloro*-3-*hydroxybut*-1-*ynyl*)-2,2′-*bithienyl* (X), plates, m. p. 55° [Found: C, 53·2; H, 3·25%; *M* (mass spectrum), 268 and 270 (ratio 2 : 1). $C_{12}H_9ClOS_2$ requires C, 53·6; H, 3·35%; *M*, 268], R_F 0·30 (system C, green), $\lambda_{max.}$ 245, 331, 336 mμ, $\nu_{max.}$ (film) 3300 (OH), 2200 (C⋮C), 1050 (CHOH), 840 (2-thienyl), 800 (thiophen-2,5-diyl), 758 (C–Cl), and 694 cm.$^{-1}$ (thiophen-2,5-diyl). N.m.r. spectrum: τ 3·0 (5, multiplet, bithienyl protons); 5·3 (1, singlet, O*H*); 6·3 (2, singlet, CH_2Cl); 6·4 (1, singlet, C*H*OH).

Further elution gave 5-(4-*hydroxybut*-2-*ynyl*)-2,2′-*bithienyl* (IX) (145 mg.), plates from n-pentane, m. p. 66—67° (Found: C, 61·6; H, 4·5; S, 26·9. $C_{12}H_{10}OS_2$ requires C, 61·5; H, 4·3; S, 27·4%), $\lambda_{max.}$ 242, 328, 334 mμ (log ε 3·82, 4·34, 4·35), $\nu_{max.}$ 1030 (CH_2·OH), 840 (2-thienyl), 800 cm.$^{-1}$ (thiophen-2,5-diyl). N.m.r. spectrum: τ 3·05 (5, multiplet, bithienyl protons); 6·2 (triplet, CH_2OH); 7·25 (3, triplet, C⋮C·CH_2 and CH_2·O*H*), R_F 0·22 (system D; orange), 0·12 (system C).

5-*Ethynyl*-2,2′-*bithienyl* (VI).—(*a*) 5-Acetyl-2,2′-bithienyl [14] (14·0 g.) was heated under reflux with phosphorus pentachloride (23·1 g.) in benzene (200 ml.) for 2 hr. The cooled solution was washed with sodium hydrogen carbonate (3 × 150 ml.), dried, and passed through a short column of alumina in pentane, to give a yellow oil (9·8 g.). This oil was dehydrohalogenated in liquid ammonia substantially as described by Bohlmann and Herbst.[12] Repeated chromatography of the product over alumina and elution with pentane–ether (95 : 5) gave 5-*ethynyl*-2,2′-*bithienyl* (VI) (737 mg.) as a yellow oil which could not be distilled, $\lambda_{max.}$ (hexane) 248, 326, 331 mμ, $\nu_{max.}$ (film) 3300 (⋮CH), 2100 (C⋮CH), 840 (2-thienyl), 800 (thiophen-2,5-diyl), 695 cm.$^{-1}$ (2-thienyl). N.m.r. spectrum: τ 2·9 (5, multiplet, bithienyl protons); 6·77 (1, singlet, C⋮C*H*), R_F 0·70 (system A, blue-green).

The *mercury derivative* obtained from aqueous ethanolic potassium mercuri-iodide solution crystallised from chloroform as plates, m. p. 204—205° (Found: C, 41·5; H, 1·7. $C_{20}H_{10}HgS_4$ requires C, 41·5; H, 1·7%), $\nu_{max.}$ 2125 (C⋮CHg).

(*b*) Phosphorus oxychloride (7·5 g.) was slowly added to a solution of 5-acetyl-2,2′-bithienyl (9·5 g.) in dimethylformamide (21 ml.) and the mixture heated on a water-bath for 3 hr. A saturated solution of sodium acetate (400 ml.) was added and the mixture extracted with ether (2 × 250 ml.). The ether was evaporated and the residue heated under reflux with potassium hydroxide (30 g.) in methanol (300 ml.) and water (20 ml.) for 2 hr. The solution was cooled, diluted, and extracted with ether (3 × 150 ml.) which was dried and evaporated to give an oil. Chromatography over alumina and elution with pentane gave 5-ethynyl-2,2′-bithienyl (4·1 g.) as a pale yellow oil, identical with the material described above.

5-(1,1-*Dichloroethyl*)-2,2′-*bithienyl* (XIV) *and* 5-*Dichloromethyl*-2,2′-*bithienyl* (XV).—5-Acetyl-2,2′-bithienyl [14] (5·0 g.) and phosphorus pentachloride (6·6 g.) in benzene (80 ml.) were heated under reflux for 2·5 hr. Working up as previously described (see above) gave a yellow oil (3·0 g.). From this point all operations were carried out under low-intensity red light. Repeated chromatography over alumina and elution with n-pentane gave (5-(1,1-*dichloroethyl*)-2,2′-*bithienyl* (XIV) (633 mg.), plates from n-pentane, m. p. 50—53°, $\lambda_{max.}$ 249, 345 mμ (log ε 4·07, 4·35), $\nu_{max.}$ 840 (2-thienyl), 800 (thiophen-2,5-diyl), 770 (C–Cl), 700 (2-thienyl), R_F 0·89 (system A, dark green). This compound was extremely unstable and we were unable to obtain satisfactory analyses (Found: C, 47·3; H, 2·8. $C_{10}H_8Cl_2S_2$ requires C, 45·6; H, 3·1%). Dehydrohalogenation with sodamide in liquid ammonia gave high yields of 5-ethynyl-2,2′-bithienyl (VI).

Further elution with n-pentane gave 5-*dichloromethyl*-2,2′-*bithienyl* (XV) (666 mg.) as plates from n-pentane, m. p. 97—98° [Found: Cl, 28·5; S, 25·2%; *M* (mass spectrum), 248. $C_9H_6Cl_2S_2$ requires Cl, 28·5; S, 27·4%; *M*, 248·3], $\lambda_{max.}$ 250, 344 mμ (log ε 3·90, 4·35), $\nu_{max.}$ 840 (2-thienyl), 804 (thiophen-2,5-diyl), 775 (C–Cl), 705 cm.$^{-1}$ (2-thienyl). N.m.r. spectrum: τ 3·0 (5, multiplet, bithienyl protons); 3·33 (1, singlet, C*H*Cl_2); R_F 0·80 (system A, dark blue).

5-(4-*Hydroxybut*-1-*ynyl*)-2,2′-*bithienyl* (IX).—5-Ethynyl-2,2′-bithienyl (1·1 g.) was treated with ethylmagnesium bromide [from magnesium turnings (168 mg.) and ethyl bromide (976 mg.) in anhydrous ether (50 ml.)]. Ethylene oxide (500 mg.) in anhydrous ether (10 ml., precooled to −15°) was added during 15 min. with stirring at −15° to give an orange complex.

The mixture was then heated under reflux for 1 hr. after which the ether was removed by distillation until a dry complex was obtained. This was decomposed with 2N-hydrochloric acid, extracted with ether (3 × 100 ml.), and the ethereal extract was worked up in the usual way to give an oil which was purified by chromatography over alumina (2 × 25 cm.). Elution with n-pentane gave unchanged 5-ethynyl-2,2′-bithienyl (650 mg.); further elution with n-pentane–ether (1 : 1) gave a fraction which was purified by further chromatography over silica gel. Elution with n-pentane–ether (1 : 1) gave 5-(4-*hydroxybut*-1-*ynyl*)-2,2′-*bithienyl* (IX) (352 mg.), plates from n-pentane, m. p. 66°, identical with the natural product.

5-(*But*-3-*en*-1-*ynyl*)-2,2′-*bithienyl* (II).—The preceding alcohol (IX) (80 mg.) in pyridine (0·6 ml.) was added to toluene-*p*-sulphonyl chloride (100 mg.) in pyridine (2 ml.) during 30 min. below 25°, and then set aside overnight. The mixture was worked up in the usual way and purified by chromatography over silica gel (10 × 1 cm.). Elution with n-pentane–ether (4 : 1) gave the *toluene*-p-*sulphonyl derivative* of (IX) as a colourless oil, (120 mg.) $\nu_{max.}$ 840 (2-thienyl), 800 cm.$^{-1}$ (thiophen-2,5-diyl); R_F 0·48 (system D, green-blue).

The toluene-*p*-sulphonyl derivative (110 mg.) in ethanol (1 ml.) was added to potassium hydroxide (200 mg.) in aqueous ethanol (1 ml.) (1 : 1 v/v) and allowed to stand at 70° for 2 hr. Chromatography of the resulting oil on alumina and elution with n-pentane gave 5-(but-3-en-1-ynyl)-2,2′-bithienyl (II) (48 mg.), identical with the natural product.

cis-5-(4-*Hydroxybut*-1-*enyl*)-2,2′-*bithienyl* (XIII).—(*a*) 5-(4-Hydroxybut-1-ynyl)2,2′-bithienyl (IX) (234 mg.) and Lindlar catalyst [33] (1 g.) in ethyl acetate (10 ml.) were shaken in darkness in an atmosphere of hydrogen until 1 mol. of hydrogen (22·4 ml.) had been taken up. The catalyst was removed and the solvent evaporated under reduced pressure to give cis-5-(4-*hydroxybut*-1-*enyl*)-2,2′-*bithienyl* (XIII) (230 mg.) as plates from pentane, m. p. 57—58° (Found: C, 61·2; H, 5·3; S, 26·6. $C_{12}H_{12}OS_2$ requires C, 61·0; H, 5·1; S, 27·4%), $\lambda_{max.}$ 243, 333—337 mμ (log ε 3·97, 4·32), $\nu_{max.}$ 3300 (OH), 1040 (CH_2·OH), 840 (2-thienyl), 800 (thiophen-2,5-diyl), 690 cm.$^{-1}$ (2-thienyl). N.m.r. spectrum: τ 2·95 (5, multiplet, bithienyl protons); 3·4—4·8 (2, multiplet, C*H*:C*H*); 6·3 (2, triplet, C*H*$_2$·OH); 7·2 (3, multiplet :CH·C*H*$_2$ and O*H*); R_F 0·29 (system D, blue-green), 0·11 (system E).

(*b*) 5-(4-Hydroxybut-1-ynyl)-2,2′-bithienyl (IX) (400 mg.) in anhydrous ether (50 ml.) at 25° was treated with diborane [from sodium borohydride (100 mg.)] in diglyme (20 ml.) in an atmosphere of nitrogen during 30 min. Glacial acetic acid (1 ml.) was added and the solution worked up by extraction with ether. The oil obtained on evaporation of the ether was purified by preparative thin-layer chromatography (system E) to give *cis*-5-(4-hydroxybut-1-enyl)-2,2′-bithienyl (XIII) (15 mg.) as plates from pentane, m. p. 57—58°, identical with the material already described.

The *trans*-isomer, m. p. 80° (lit.,[12] 79°), was prepared, and when compared directly with the *cis*-isomer showed $\lambda_{max.}$ 245, 339—341 mμ (log ε 3·94, 4·31), R_F 0·29 (system D, blue green).

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[33] R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955, p. 200.