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BITHIENYL DERIVATIVES FROM *TAGETES MINUTA* L.

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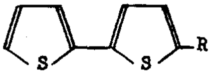
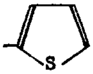
In an investigation prompted by the observation of nematicidal activity in *Tagetes minuta* L. (1) we have examined the thiophene derivatives which are present in the roots. We have isolated α-terthienyl (I) and 5-(but-1-en-3-ynyl)-2,2'-bithienyl (II), which have previously been obtained from *Tagetes patula* and *T.erecta* (2). We have, however, been unable to obtain cis-5-(1-acetoxy-but-3-enyl)-2,2'-bithienyl (III) which was isolated by Bohlmann and Herbst (2) from the same two species.



(I) R= 

(II) R= $-C{\equiv}C-CH{=}CH_2$

(III) R= $-CH{=}CH-CH_2-CH_2OAc$

(IV) R= $-CH{=}CH-CH_2-CH_2OH$

(V) R= $-C{\equiv}C-CH_2-CH_2OH$

(VI) R= $-C{\equiv}C-CHOH-CH_2Cl$

(VII) R= $-C{\equiv}C-MgBr$

(VIII) R= $-I$

(IX) R= $-C{\equiv}C-CHCl-CH_2OH$

Two other new bithienyl derivatives have been obtained from *T.minuta*; these have been identified as 5-(but-1-ol-3-ynyl)-2,2'-bithienyl (V) and 5-(but-1-chloro-2-ol-3-ynyl)-2,2'-bithienyl (VI). Compound (V), m.p. 67°, gave an analysis for $C_{12}H_{10}OS_2$; the infrared spectrum showed a monosubstituted bithienyl residue (840, 800 cm.$^{-1}$) and a primary -OH group (3300, 1050 cm.$^{-1}$) but no -CH=CH- or -C≡C- absorption, whereas the ultraviolet spectrum (λ_{max} 242, 328, 334 mμ log ε 3.82, 4.34, 4.35) indicated an unsaturated chromophore adjacent to the bithienyl residue. This anomaly was resolved by the N.M.R. spectrum which showed resonances at 3.05 (5 protons, bithienyl residue); 6.2 (2 protons, triplet, $-CH_2$); and 7.25 (3 protons, broad triplet, $-CH_2$, $-OH$). No resonances appeared for olefinic protons so that the conjugation appeared to be acetylenic. The absence of an absorption for this group in the infrared spectrum is not unusual (3).

The compound (V) was synthesised by treating the acetylenic Grignard (VII) with ethylene oxide. It was also prepared in high yield by reaction between 5-iodo-2,2'-bithienyl (VIII) (4) and the cuprous salt of but-3-yn-1-ol, by heating under reflux in pyridine in an atmosphere of nitrogen. The latter method which is similar to that recently described (5) for aromatic acetylene derivatives seems to be of general application for the synthesis of heterocyclic acetylenes. We have numerous examples (6) of syntheses of this type, e.g. the derivative (II) can be obtained under the same conditions in one step using the cuprous salt of vinylacetylene.

The synthetic material was identical with the natural product but the physical constants and spectral data were identical with those recorded (2) for the naturally-occurring alcohol (IV). However, comparison of the crude root extracts of the three species mentioned by thin-layer chromatography (7) showed a remarkable similarity. Since the evidence (2) originally advanced for (IV) was ambiguous we synthesised (IV) by stereospecific reduction with diborane of the acetylenic carbinol (V). The <u>cis</u> olefinic carbinol (IV) had m.p. 58° (λ_{max} 243, 335 mμ) whereas the <u>trans</u> isomer synthesised by the method of Bohlmann and Herbst (2) had m.p. 78° (λ_{max} 245, 339-341 mμ). The properties of the <u>cis</u>-isomer are not consistent with those of the stable compound assigned this structure by Bohlmann (2). Furthermore, the <u>cis</u> isomer proved very labile and isomerised readily to the <u>trans</u>. We suggest that the compound isolated by Bohlmann (2) is the acetylenic carbinol (V).

The synthesis of the carbinol (V) provided a simple method for the preparation of the en-yne (II). Conversion to the p.tosyl derivative and elimination with sodium hydroxide gave (II), in high yield, identical with natural material.

Structure (VI) for the second bithienyl derivative, m.p. 55°, (2.8 mg.) was supported by CH analysis, indicating $C_{12}H_9S_2OCl$; the infrared spectrum 3300 cm.$^{-1}$ (-OH); 2200 cm.$^{-1}$ (-C≡C-); 840, 800 cm.$^{-1}$ (mono-substituted bithienyl residue); 758 cm.$^{-1}$ (-C-Cl); the ultraviolet absorption maximum 245, 336 mμ (conjugated bithienyl) and the mass spectrum. This showed a parent molecular ion at 268 which lost fragments of 49 mass units ($-CH_2Cl$) and 17 mass units (-OH) to give ions of mass number 219 and 251. This supported structure (VI) rather than the alternative (IX). Reaction of the acetylenic Grignard (VII) with chloroacetaldehyde gave an oil with spectral properties (I.R. and U.V.) and behaviour on thin-layer chromatography which was identical with natural material. We have not been able to obtain crystalline material despite rigorous purification. It is likely that the natural material is optically active, (lack of material has precluded any determinations), and that the racemic synthetic material has a much lower melting point. Attempted resolution is in progress.

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