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Studies Related to Naturally Occurring Acetylene Compounds, XXVI. The Synthesis of 5-(1-propynyl)-2-formylthiophene, Junipal, and *trans* Methyl 5-(1-propynyl)-2-thienylacrylate

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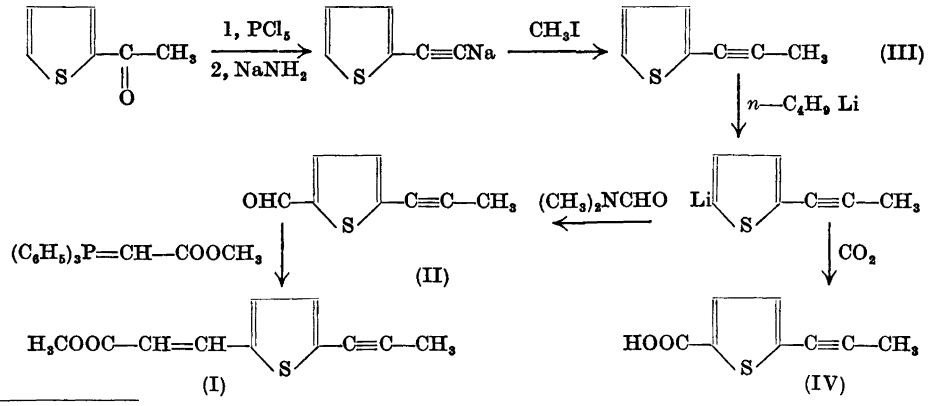
The synthesis is described of junipal (II), a metabolic product from a wood-rotting fungus, and also of *trans* methyl 5-(1-propynyl)-2-thienylacrylate (I), the steric isomer of a naturally occurring substance isolated from a *Compositae* plant.

In the previous communication of this series [1] Guddal and Sörensen described the isolation of a naturally occurring thiophene derivative from the root of Tancy (= *Chrysanthemum vulgare* Bernh.) of the *Compositae* family. The compound was deduced as *cis* methyl 5-(1-propynyl)-2-thienylacrylate (I) on the basis of analysis, characterisation of the hydrogenation product and evidence obtained from ultraviolet- and infrared spectra.

In order to confirm this structure the synthesis of (I) was undertaken through the following route:



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An intermediate in this synthesis, *viz.* 5-(1-propynyl)-2-formylthiophene (II), has the same structure as that proposed for junipal, a metabolic product isolated by Birkinshaw and Chaplen [2] from the wood-rotting fungus *Daedalea juniperina* Murr.

2-Thienylacetylene was prepared from 2-acetylthiophene by chlorination with phosphorus pentachloride and subsequent dehydrochlorination with sodium amide in liquid ammonia, in the way described by Vaitiekunas and Nord [3]. The ethynyl compound was not isolated but reacted further, as the sodium salt, with methyl iodide to give 2-(1-propynyl)-thiophene (III) in 30 % overall yield. The compound turned dark brown fairly rapidly, when stored at room temperature. With butyl lithium in ether (III) readily formed a lithium derivative. The lithium is most probably substituted in the 5-position. This is analogous to previous results from this reaction with thiophenes [4], and it is also in agreement with kinetic measurements [5,6]. Reaction of the lithium compound with N-dimethylformamide [7] gave the corresponding aldehyde (II) in 21 % yield, as almost colourless crystals, m.p. 81—82°. A good deal of polymeric material was formed. The ultraviolet- and infrared spectra were in agreement with those published for junipal [2], and a mixed melting point determination with the natural substance, kindly provided by Professor J.H. Birkinshaw, showed no depression.

Carbonation of the lithium derivative yielded 2-(1-propynyl)-thiophene-5-carboxylic acid (IV), = junipic acid [2].

The aldehyde (II) readily underwent a Wittig reaction [8] with methylcarbethoxytriphenylphosphonium chloride. From the reaction mixture the wanted ester (I) was obtained in 55 % yield as colourless needles, m.p. 77°. The band at 962 cm^{-1} in the infrared spectrum strongly indicated that the configuration about the double bond was *trans*.[9] The compound was found to be in all respects identical with the photo-isomerised naturally occurring substance [1]. Theoretically the *cis*-isomer should also be formed in the Wittig reaction, and this has been confirmed in some instances [8,10]. We were not able, however, to isolate any of the *cis*-isomer from our reaction mixture.

Birkinshaw and Chaplen [2] also reported the isolation of a second thiophene derivative, accompanying junipal. They were only able to obtain it pure as the 2,4-dinitrophenylhydrazone. The analysis and ultraviolet spectrum pointed to a structure similar to junipal, but with an additional double bond. It was suggested [11] that the substance was the aldehyde corresponding to the ester(I), *viz.* 2-(1-propynyl)-5-thienylacraldehyde. The synthesis of this aldehyde, however, showed that this unfortunately was not so. Further work on the structure of this metabolic product is in progress.

EXPERIMENTAL

All melting points are uncorrected. The carbon-hydrogen analyses were carried out by Alfred Bernhardt, Mühlheim, Ruhr, Germany.

2-(1-Propynyl) thiophene (III). The sodium salt of 2-ethynylthiophene in liquid ammonia was prepared from 75 g of 2-acetylthiophene according to the method of Vaitiekunas and Nord [3]. Methyl iodide (70 g) was then added over a period of 25 min and the mixture was stirred overnight. 400 ml of water were carefully added and the dark brown solution extracted with ether. The extract was washed with water and dried over anhydrous sodium sulphate. The ether was removed under vacuum, and the residue purified by chromatography on deactivated alumina (1 % water). A yellow oil was eluted

with light petroleum and fractionation of this gave 22.0 g (30 % from acetylthiophene) of 2-(1-propynyl) thiophene as a colourless liquid, b. p. 65—66°/7 mm, n_D^{17} 1.5950. (Found: C 69.05; H 4.75. Calc. for C_7H_6S: C 68.81; H 4.95.) Ultraviolet absorption, in ethanol: λ_{max} 267.5 mμ; log ε 3.82.

5-(1-Propynyl)-2-formylthiophene, junipal (II). 2-(1-propynyl) thiophene (III) (1.3 g) was dissolved in 10 ml of dry ether, and 9.6 ml of a 1.1 N butyl lithium solution in ether was added with stirring. After 15 min at room temperature the red-coloured solution was cooled to −10° and 0.8 g of N-dimethylformamide in 2 ml of dry ether was added with stirring. The mixture was allowed to attain room temperature (15 min) and then decomposed with a saturated aqueous solution of ammonium chloride. Extraction with ether, drying and evaporation of the solvent under vacuum gave a crystalline residue. Recrystallisation from light petroleum-ether yielded the aldehyde (330 mg, 21 %), m. p. 79—81° as slightly yellow-coloured needles. Almost colourless crystals were obtained by sublimation at 50°/0.4 mm, m. p. 81—82°. (Found: C 63.87; H 4.11. Calc. for C_8H_6OS: C 63.97; H 4.03.) Ultraviolet absorption, in ethanol: λ_{max} 286 and 320 mμ; log ε 3.91 and 4.27, respectively. Birkinshaw and Chaplen [2] report m. p. 80°. Ultraviolet absorption in ethanol: λ_{max} 216.5, 286.5 and 320 mμ; log ε 3.73, 3.95 and 4.29, respectively. A 1:1 mixture with the natural substance melted at 80—81.5°.

5-(Propynyl) thiophene-5-carboxylic acid (IV). 2-(1-Propynyl) thiophene(III) (2.0 g) was dissolved in 10 ml of dry ether, and 14.5 ml of a 1.13 N solution of butyl lithium in ether was added with stirring. After 15 min at room temperature the solution was poured into a stirred slurry of solid carbon dioxide and dry ether. When the excess carbon dioxide had evaporated, water was added and the organic phase separated. The aqueous phase was acidified with dilute hydrochloric acid and extracted with ether. Evaporation of the solvent and recrystallisation of the residue from light petroleum-ether gave the acid (1.1 g; 37 %) as yellow needles, m. p. 175—177°. Further purification by sublimation and recrystallisation raised the melting point to 176.5—177.5°. (Found: C 57.65; H 4.20. Calc. for $C_8H_6O_2S$: C 57.80; H 3.60.) Ultraviolet absorbtion, in ethanol: λ_{max} 293 mμ; log ε 4.02. Birkinshaw and Chaplen [2] record m. p. 180°.

Methyl 5-(1-propynyl)-2-thienylacrylate (I). Methylcarbethoxy-triphenyl-phosphonium chloride (550 mg) was dissolved in 2 ml absolute methanol, and 8.0 ml of a 0.185 N solution of sodium methoxide was added with stirring. After 30 min at room temperature, 215 mg of 5-(1-propynyl)-2-formylthiophene (II) was added with stirring. The solution was left at room temperature for 40 h. The methanol was distilled under vacuum, and the residue extracted with ether. The extract was washed with 2 N hydrochloric acid, then with water and finally dried over magnesium sulphate. Chromatography on neutral alumina and subsequent recrystallisation from light petroleum yielded the ester (I) (156 mg; 55 %) as colourless needles, m. p. 77°. (Found: C 64.19; H 5.09. Calc. for $C_{11}H_{10}O_2S$: C 64.05; H 4.89.) Ultraviolet absorption, in ethanol: λ_{max} 235 and 341.5 mμ; log ε 3.98 and 4.50, respectively.

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