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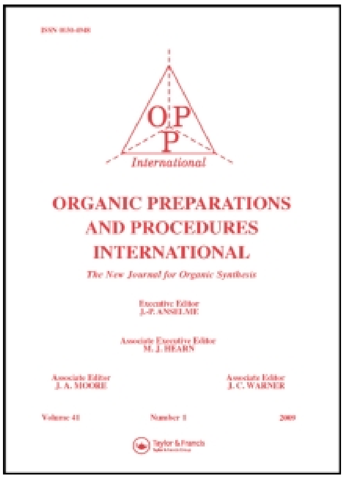

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A SYNTHESIS OF TAIWANIN C

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A SYNTHESIS OF TAIWANIN C

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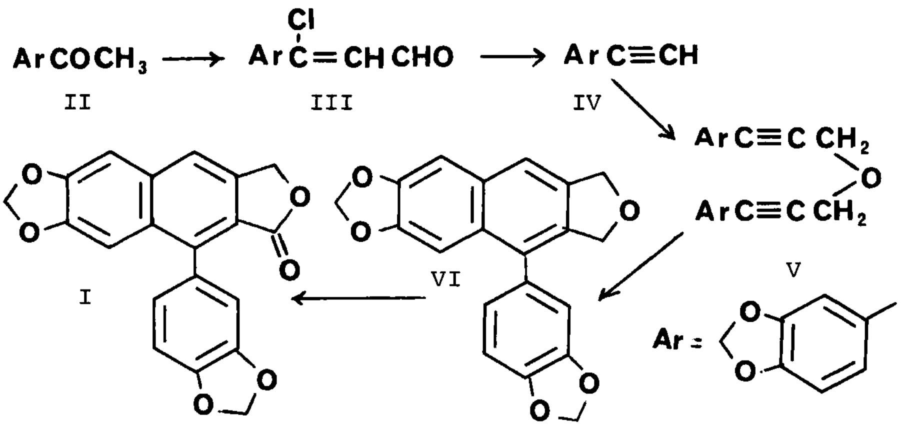
The structure 6,7-methylenedioxy-1-(3',4'-methylenedioxyphenyl)-3-hydroxymethylnaphthalene-2-carboxylic acid lactone (I) was proposed[1] for taiwanin C, an extractive of the heartwood <u>Taiwania cryptomeriodes</u> Hayata.[2] Although this compound had been synthesized three decades prior to its isolation as a natural product,[3] a comparison specimen was unavailable. We reported an independent synthesis of I which confirmed the structure,[4] and now describe a brief alternative synthesis based on the cyclization of an appropriate bis-phenylpropynyl ether and oxidation of the resulting phenylnaphthalene dihydrofuran.



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3,4-Methylenedioxyphenylacetylene (IV) was prepared by the Vilsmeier reaction on 3,4-methylenedioxyacetophenone (II) followed by hot aqueous base treatment of the β-aryl-β-chloroacrolein (III).[5] Treatment of the lithium arylacetylide with bis(chloromethyl)ether gave the bis-methylenedioxyphenylpropynyl ether (V) which was converted to the phenylnaphthalene (VI) by the action of potassium t-butoxide.[6] We had shown earlier that oxidation of the dihydrofuran ring of the unsubstituted model compound with Jones reagent yielded a mixture of two lactones.[7] Under these conditions VI gave no identifiable product, but with chromic acid in pyridine-methylene chloride[8] yielded the lactone (I) identified as taiwanin C by direct comparison.

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EXPERIMENTAL

Bis[3-(3′,4′-methylenedioxyphenyl)-2-propynyl] ether (V). - The Vilsmeier reagent (prepared from 8.0 g. of phosphorus oxychloride and 8.0 ml. of dimethylformamide) at 0° was added to a solution of 3,4-methylenedioxyacetophenone (3.3g) in dimethylformamide (20 ml) and the mixture was heated at 60° for 4 hr. After having been stirred overnight at room temperature the reaction mixture was poured into an aqueous solution (200 ml) of sodium acetate (25 g) and ammonium chloride (30 g). The precipitate was collected and crystallized once from ether to give 3-chloro-3-(3′,4′-methylenedioxyphenyl)prop-2-enal (III) as a very pale yellow solid (2.5 g), mp. 104-107°. δ($CDCl_3$) 6.06 (s, 2H, $-OCH_2O-$), 6.56 (d, J = 7 Hz, 1H, C=CH), 6.86 (d, J = 8 Hz, 1H, H-5), 7.20 (d, J = 1.5 Hz, 1H, H-2), 7.37 (dd, J = 8,1.5 Hz, 1H, H-6) and 10.17 (d, J = 7 Hz, 1H, CHO).

Without further purification, a solution of 6.4 g. of III in dioxane (200 ml) was added dropwise to a well-stirred hot solution of sodium hydroxide (15 g) in water (100 ml) and stirred at 80° for 1 hr. The mixture was then concentrated under reduced pressure, cooled and extracted with ether. The washed and dried ethereal extract was then evaporated to give 3,4-methylenedioxyphenylacetylene (IV) as a pale yellow oil (4 g). δ($CDCl_3$): 2.96 (s, 1H, $C\equiv CH$), 5.96 (s, 2H, $-OCH_2O-$), 6.6-7.1 (m, 3H, ArH), ν (neat) 2100 (w) and 3200 (m) cm^{-1}.

To a solution of 1.46 g. of the acetylene (III) in dry tetrahydrofuran (20 ml) at -30° was added a molar equivalent of 1.9 M methyllithium in ether and the mixture stirred until gas evolution ceased. A solution of bis(chloromethyl) ether (0.57 g) in ether (20 ml) was then added slowly, the temperature allowed to rise to room temperature and the mixture stirred for 8 hr. The solvents were then removed under reduced pressure, the residue extracted by water and ether and the washed and dried ethereal extract was evaporated and crystallized from ethanol to give bis[3-(3′,4′-methylenedi-

CAUTION: Bis(chloromethyl) ether is a POTENT carcinogen and should handled with appropriate safety precautions.

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oxyphenyl)-2-propynyl]ether (V) as needles (0.9 g), mp 103-105°, δ($CDCl_3$) 4.48 (s, 4H, $-CH_2-$), 5.95 (s, 4H, $-OCH_2O-$), 6.5-7.0 (m, 6H, ArH).

Anal. Calcd. for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22.

Found: C, 71.5; H, 4.2%.

6,7-Methylenedioxy-1-(3′,4′-methylenedioxyphenyl)-3-hydroxymethylnaphalene-2-carboxylic acid lactone (Taiwanin C) (I). - A solution of the ether (V, 0.2 g) in t-butanol (20 ml) was added to a freshly prepared solution of potassium t-butoxide (from 4 g K) in t-butanol (80 ml), the mixture heated at 80° for 4 hr, the solvent removed and the residue extracted with ether and water. The washed, decolorized and dried ethereal extract on evaporation gave crude 4-(3′,4′-methylenedioxyphenyl)-6,7-methylenedioxy-1,3-dihydronaphtho[2,3-c]furan (VI). δ($CDCl_3$) 4.96 (s, 2H, $3-CH_2$), 5.02 (s, 2H, $1-CH_2$), 5.83 (s, 2H, $-OCH_2O-$), 6.01 (s, 2H, $-OCH_2O$) and 6.5-7.6 (m, 6H, ArH).

To a solution of crude VI (0.2 g) in methylene chloride (50 ml) was added the complex from chromium trioxide (0.6 g) and pyridine (2 g) and the mixture stirred at 50° for 4 hr and then at room temperature for 72 hr. The brown precipitate which was formed was collected and the filtrate washed with 2N hydrochloric acid and water. The precipitate was extracted with hot acetone and the extract added to the

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filtrate, which was then decolorized and evaporated to give a yellow oil which crystallized upon trituration with chloroform-light petroleum. Recrystallization from chloroform gave taiwanin C (I) (35 mg), mp 269-272°, whose ir and pmr spectra were identical to those of an authentic specimen.

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