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SYNTHESIS OF YANGONOLE

R. D. Stipanovic and G. J. Calton

Department of Chemistry, Texas A&M University
College Station, Texas 77843

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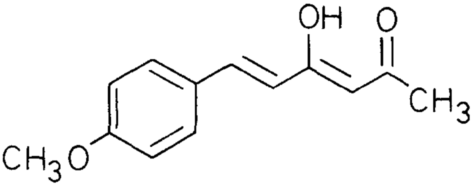
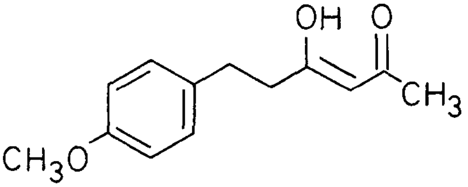
For sysnthtic studies under investigation it was necessary to prepare several p-substituted anisyl derivatives. Of these yangonole (I)(1), and its dihydroderivative (II) were in pressing demand.



(I)



(II)

Although several alternate schemes were possible, Hauser's (2) procedure for the production of dianions from β-diketones was the most promising. Thus, p-anisaldehyde (40 g) was added dropwise to the dianion of acetylacetone (30 g) generated with sodium amide, from 13.8 g of sodium. The crude reaction product was dissolved in methanol (500 ml) and heated to reflux. Concentrated hydrochloric acid (10 ml) was added and reflux continued for one hour. On work up, the base soluble fraction afforded a yellow crystalline compound (10-20%) which proved to be yangonole, m.p. 91-92° (Lit. (1) 92-93°). The copper complex of yangonole was prepared, m.p. 235.5-236.5° (3). The nmr spectrum exhibited the following peaks (CCl_4): singlet at δ15.08 (enol), $A_2'B_2'$ multiplet centered at δ7.11 (aromatic), AX doublet at δ7.45 and δ6.18 (vinyl J $\simeq$ 16 cps), singlet at δ5.48 (methine proton of enol), singlet at δ3.79 (methoxy), and a singlet at δ2.06 (methyl ketone). The UV spectrum showed the following peaks: $\lambda_{max}^{CH_3OH}$ 349 nm (ε=27,000), 239 nm (ε=11,650), 204 nm (ε=13,260). Yangonole (1.5 g) was cleanly reduced (85%), at atmospheric pressure, with 5% palladium on carbon (40 mg) in methanol (50 ml). The reaction was stopped when the uptake of hydrogen had essentially ceased and the solution, after the catalyst had precipitated, was colorless. The sole product was 5,6-dihydroyangonole (II) (copper derivative, m.p. 179.5-180°). The dihydroderivative was prepared directly in much higher yields (50-80%), by the dropwise addition of *p*-methoxybenzyl chloride (156 g) to the dianion of acetylacetone (124 g) generated with sodium amide from 75.9 g of sodium (4). The melting point, mixed melting point, ir and nmr of dihydroyangonole preprepared by this method was identical with that prepared by the reduction of yangonole. Dihydroyangonole exhibited the following nmr spectrum (CCl_4); singlet at δ15.16 (enol), $A_2'B_2'$ quartet centered at δ6.82 (aromatic), singlet at δ5.33 (methine proton of enol), singlet at δ3.61 (methoxy), multiplet δ2.2-2.9 (four methylene protons), and a singlet at δ1.90 (methyl ketone).

Dihydroyangonole was prepared in an alternate procedure by acylation of 1-(*p*-methoxyphenyl)-3-butanone (5) with sodium hydride and ethyl acetate. However, the desired methyl acylated product was contaminated with considerable quantities (25% as determined by gas chromatography) of the methylene acylated product.

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