

SYNTHESIS OF TANSHINONE-II AND CRYPTOTANSHINONE

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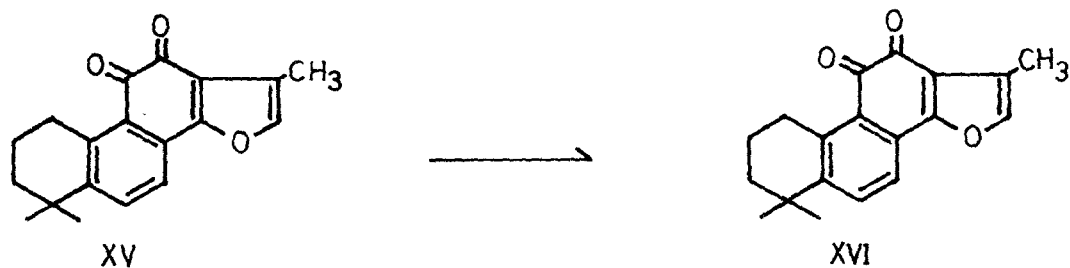
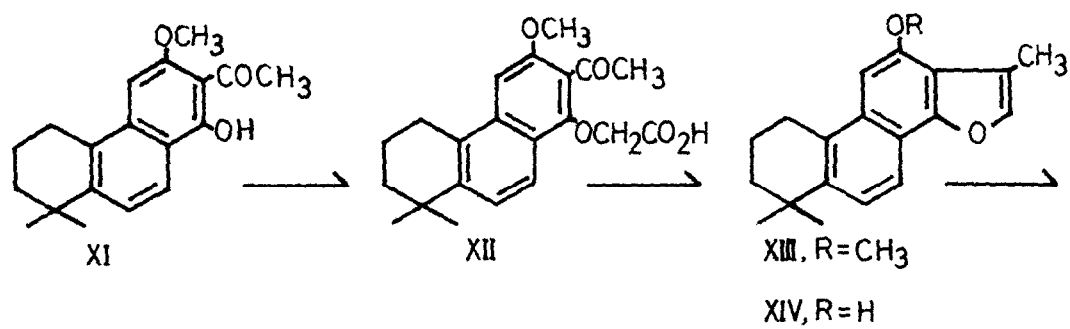
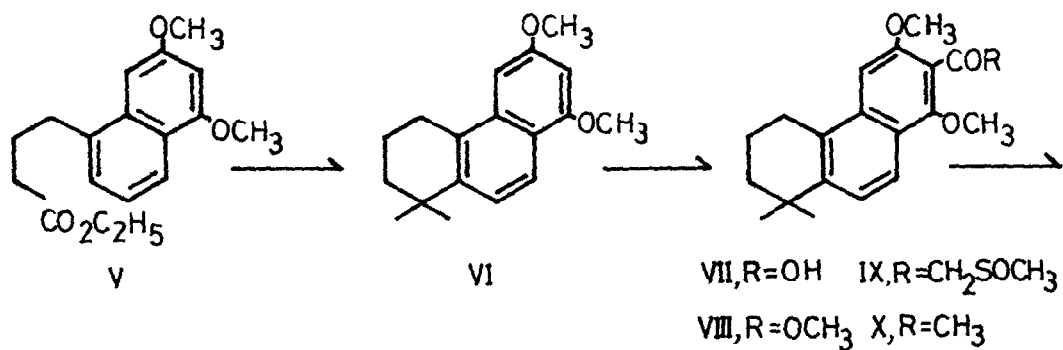
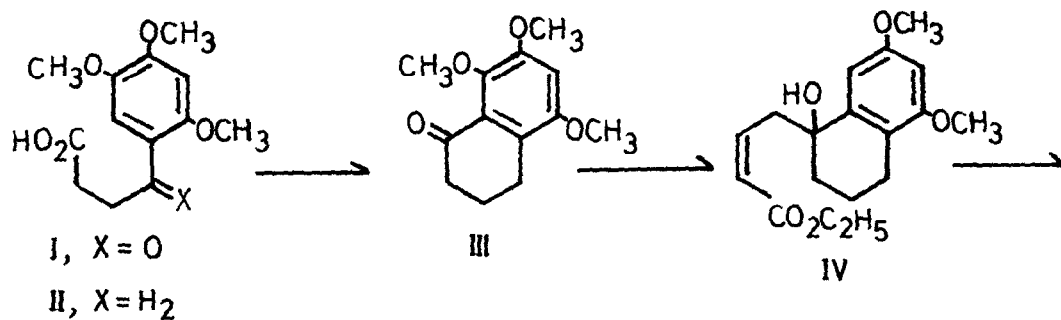
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Many tanshinones, diterpenoid pigments possessing a furonaphthoquinone, were isolated from the roots of Salvia miltiorrhiza Bunge and their structures have been determined(1) by Austrian and Japanese chemists. The total syntheses of these pigments were attempted (2) since 1961 and recently three tanshinones were synthesized by Thomson (3). In this communication we wish to report the synthesis of tanshinone-II and cryptotanshinone (4).

Catalytic hydrogenation of 2,4,5-trimethoxybenzoylpropionic acid(I) in the presence of palladized charcoal and perchloric acid afforded the trimethoxy-phenylbutyric acid(II), m.p. 62-64°, which was converted by polyphosphoric acid into the trimethoxy- α -tetralone(III), m.p. 106°, ν_{\max}^{CHF} 1680 cm^{-1} . The tetralone (III) was condensed with ethyl γ -bromocrotonate by a Reformatsky reaction, and the initial product(IV) was directly converted by dehydration and rearrangement on heating with palladized charcoal into the naphthylbutyric ester(V), m.p.69°, M^+ 302.

Reaction of the ester(V) with methylmagnesium iodide and cyclodehydration of the resulting alcohol with sulfuric acid gave the tetrahydrophenanthrene(VI), m.p.158°, M^+ 270, $\lambda_{\max}^{\text{EtOH}}$ 238, 284, 295, 331 μ . The elementary analyses and the



spectral properties, including the mass spectra, of the compounds V and VI showed that, in the Reformatsky reaction of the trimethoxy- α -tetralone(III), one of three methoxy groups was replaced by a hydrogen atom. The position of the removed methoxy group was revealed from the n.m.r. spectrum of the dimethoxytetrahydrophenanthrene(VI). The n.m.r. spectrum showed a pair of meta-coupling doublets at 6.85($J=2$ cps) and 6.51ppm($J=2$ cps) besides a 2-proton AB-quartet(8.05 and 7.37ppm, $J=8$ cps) in the aromatic proton region. This indicated that a methoxy group at C₄ was replaced by a hydrogen atom and the structure VI was assigned for the dimethoxytetrahydrophenanthrene.

Treatment of the dimethoxytetrahydrophenanthrene(VI) with butyllithium and thereafter with carbon dioxide afforded the acid(VII), which was isolated as the methyl ester(VIII), m.p. 132°, ν_{\max}^{chf} 1720cm⁻¹. The carbomethoxy group of VIII was converted by the Corey's method(5) via the sulfoxide(IX) into the methyl ketone(X), m.p. 113°, ν_{\max}^{chf} 1700cm⁻¹. One of two methoxy groups of the acetyl-dimethoxyphenanthrene(X) was selectively demethylated by treating with boron trichloride to give the acetylmethoxyphenanthrol(XI), m.p. 194°, ν_{\max}^{chf} 1620cm⁻¹.

Reaction of the acetylmethoxyphenanthrol(XI) with ethyl bromoacetate in the presence of potassium carbonate followed by base hydrolysis afforded the acid(XII), m.p. 178°, which was converted into the furophenanthrene(XIII), m.p.178°, n.m.r. 8.63(s 6H) 7.58(d 3H) 6.06ppm(s 3H), by refluxing with acetic anhydride and sodium acetate.

Hydrolysis of a methoxy group of the acid-unstable furophenanthrene(XIII) was accomplished by heating with methylmagnesium iodide at 180° to give the furophenanthrol(XIV). The furophenanthrol(XIV) was hardly oxidized by the Fremy's salt (6), but smoothly oxidized in the air to give orange crystals, which was shown to be identical to natural tanshinone-II(XV) in all respects (mixed melting point, IR- UV- and n.m.r. spectra). Previously tanshinone-II had been transformed (1) into cryptotanshinone(XVI), and then synthesis of the latter was accomplished.

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