

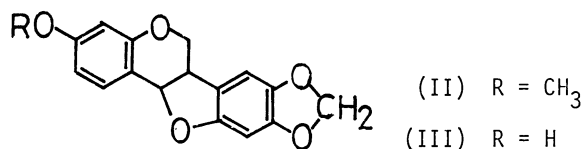
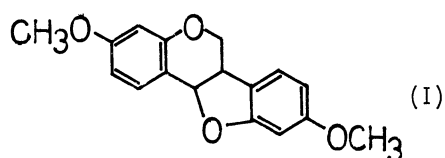
NEW SYNTHESIS OF *trans*-ISOFLAVAN-4-OL

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trans-Isoflavan-4-ol was synthesized from chromene with phenylpalladium chloride in one step. Treatment of the alcohol with NBS gave isoflavone.

Isoflavan-4-ols situate at the lower oxidation level than isoflavanones and are considered to be the key substances in the biogenetic synthesis of chromanocoumaran type compounds.¹⁾ The representative natural products having chromanocoumaran structure are homopterocarpin (I), pterocarpin (II), and maackiain (III).²⁾



trans-Isoflavan-4-ols have been synthesized by the reaction of 4-aminoisoflavan hydrochlorides with nitrous acid or by the hydroboration of isoflavenes.³⁾ However, the reduction of isoflavones or isoflavanones gave only *cis*-isoflavan-4-ols.⁴⁻⁶⁾

We have reported the hydroxyphenylation of the conjugated olefins, such as indene and 1,2-dihydronaphthalene with phenylpalladium chloride in aqueous protic solvents.⁷⁾ The addition of phenyl group and anion part of protic solvent to the olefinic double bond conjugated with benzene ring was achieved in a good yield. The configuration of the entering groups, hydroxyl group and phenyl group of the isolated product was *trans*.

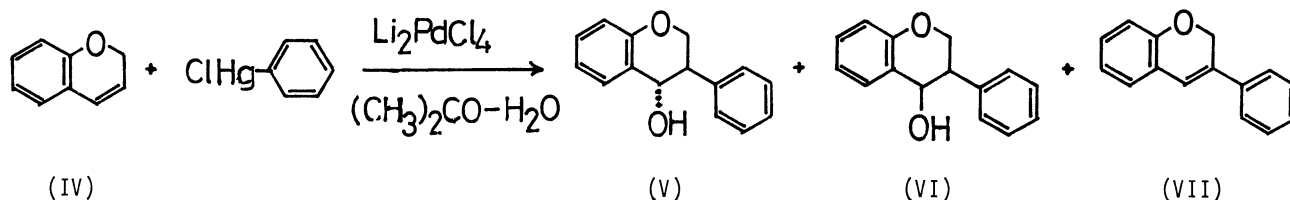
The same reaction of acenaphthylene gave also *trans*-2-phenylacenaphthenol in a reasonable yield.⁸⁾

We now report the application of this new reaction to chromene (IV) which gave *trans*-isoflavan-4-ol (V) in a high yield.

A solution of chromene (IV)⁹⁾ (3.3 mmol), lithium palladium chloride¹⁰⁾ (3 mmol) and phenylmercuric chloride (3 mmol) in a mixture of 20 ml of acetone and 10 ml of water was stirred for 4 hours at room temperature. The reaction mixture was poured into water (100 ml), the precipitated palladium was separated by filtration and the solvent was extracted with benzene (100 ml x 4). The extract was dried and the solvent was removed. Recrystallization of the residual oil from n-hexane gave needles

of mp 101°C (51%), which showed no depression of melting point when admixed with an authentic *trans*-isoflavan-4-ol. Infrared absorption spectrum, ultraviolet spectrum, and nmr spectrum of the product were identical with those of the authentic sample. The chromatography of the mother liquid on silica gel with n-hexane gave further *trans*-isoflavan-4-ol (10%). The yield of the isolated product was 61%.

Thin layer chromatography was applied to the detection of the products in the benzene extract over silica gel with a mixture of benzene and tetrahydrofuran (10 : 1), and *trans*-isoflavan-4-ol (V) (Rf 0.57), *cis*-isoflavan-4-ol (VI) (Rf 0.64), and isoflavene (VII) (Rf 0.91) were identified.



Analysis of the products by gas-chromatography on a column of PEG 20 M (1.5 meter) at 200°C showed that the products have the ratio of 1.2% of isoflavene, 93.4% of *cis*- and *trans*-isoflavan-4-ols and 5.3% of unknown product. Although the peaks of *cis*- and *trans*-isoflavan-4-ols on the gas-chromatogram were not separated completely, the separation of peaks became almost complete after trimethylsilylation of the products with a pyridine solution of hexamethyldisilazane and trimethylchlorosilane, and the ratio of *cis* to *trans* was shown to be 18.7% to 81.3%.

The solution of the *trans* alcohol (V) (0.5 mmol) and NBS (1.1 mmol) in carbon tetrachloride (10 ml) was refluxed gently for 3 hours. After separation of succinimide and evaporation of the solvent, the residual oil was treated with sodium acetate in acetic acid for 30 minutes. The reaction mixture was poured into water. The precipitate was dried and recrystallized from n-hexane. The product of mp 133°C, in 65% yield, showed no depression of melting point when admixed with a sample of authentic isoflavone.^{11, 12)}

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