Stereospecific Formation of *trans*-Phenylcoumarans by Dehydrogenative Dimerisation of *trans*- and *cis*-Isoeugenol

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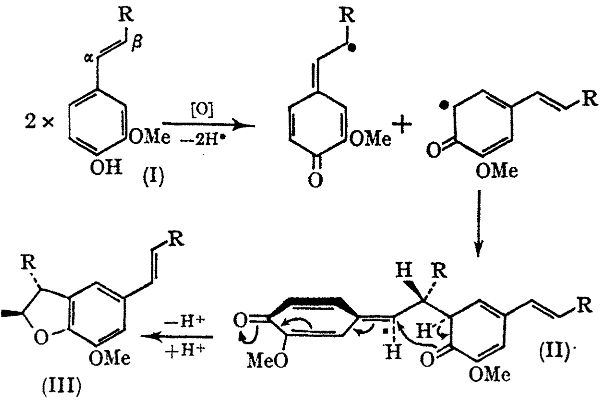
Summary *trans*- and *cis*-Isoeugenol have been oxidised to phenylcoumarans with the same stereochemistry about the hydrofuran ring.

PHENYLCOUMARANS (IIIa—c) have been obtained by free-radical oxidation of β-substituted-*p*-vinylguaiacols (Ia—c).[1] From (I) with a *trans*-configuration about the ethylenic double-bond, the resulting phenylcoumarans have the substituents at C-2 and C-3 *trans* to one another as demonstrated for (IIIa) by oxidative degradation,[2] and confirmed for (IIIb and c) by conversion into (IIIa).[1b,c] Harkin[3] has suggested that the lack of *cis*-phenylcoumaran formation may be because cyclisation of intermediate (II) to (III) is faster than rotation about the C-α–C-β bond. We have observed formation of *trans*-phenylcoumarans exclusively from *cis*- and *trans*-isoeugenol (IV) and (Ia).

Treatment of *trans*- and *cis*-isoeugenol with hydrogen peroxide (3%; 0·52 mole) in aqueous acetone containing peroxidase gave mixtures of dimeric products from which (IIIa) (65%) from *trans*-isoeugenol and (Va) (22%) (m.p. 83—84°) from *cis*-isoeugenol were obtained after chromatographic separation on silica gel. Hydrogenation of (Va) with 5% Pd–C in ethanol yielded (Vb) (95%), identical with the hydrogenation product of (IIIa).[4]

Reaction of (Vc)[1a] with 2,3-dichloro-5,6-dicyanobenzoquinone in boiling benzene for 20 hr.[5] afforded, after silica gel chromatography, the phenylcoumarone (VI) (35%) m.p. 91·5—92·5°.[6] Catalytic hydrogenation of (VI) with

5% Pd–C in absolute ethanol for 7 days at 20° (1 atm.) gave the *cis*-phenylcoumaran (VII)[7] as an oil. The n.m.r. signals peculiar to (VII) were found to be completely absent in the spectra of the oxidation product mixtures from both *trans*- and *cis*-isoeugenol.

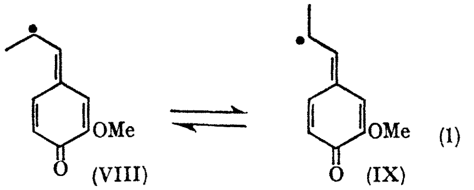


(I) (II) (III)

Ar=guaiacyl

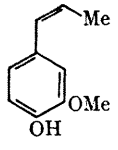
(a) R=Me; (b) R=CH_2OH;(c) R=CO_2Et

The retention of the *cis*-propenyl side-chain in (Va) and the diminished yield of (Va) in the coupling reaction [*cf.* (IIIa)] shows that the *cis*-radical (VIII) reacts as a distinct entity, and that the equilibration to the more stable *trans*-radical (IX) [equation (1)] is a slow process compared with radical coupling. Furthermore, because of the exclusive formation from (IV) of (Va) with *trans*- C-2 and C-3 substituents, a rotation about the C-α–C-β bond of the initially formed intermediate (X) (R = *cis*-propenyl) prior to cyclisation, relieving the steric compression of adjacent *cis*-methyl and quinonemethide moieties, must be invoked. Thus, the lack of formation of *cis*-phenylcoumarans from *cis*- and *trans*-substituted *p*-vinylguaiacols is due the equilibrium [equation (2)] favouring (II), rather than to the rapidity of the cyclisation process.[4]

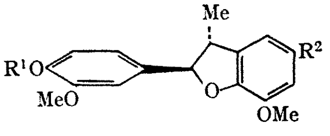


(VIII) (IX) (1)

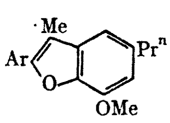
$$\text{(II)} \rightleftharpoons \text{(X)} \qquad (2)$$



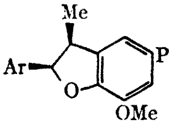
(IV)



(V) a; R^1=H, R^2=*cis*-CH:CHMe
b; R^1=H, R^2=Pr^n
c; R^1=Me, R^2=Pr^n

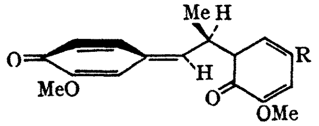


(VI)



(VII)

Ar=3,4-dimethoxyphenyl



(X)

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