The Natural Occurrence of *cis*- and *trans*-Cinnamylphenols

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BIOGENETIC proposals[1] for the formation of neoflavanoids[2] by the cinnamylation of phenols (or their polyketide equivalents) suggested that the natural co-occurrence of neoflavanoids and cinnamylphenols was to be expected.[1] We report the natural occurrence and constitutions of nine cinnamylphenols (Table). These cinnamylphenols represent a new class of natural products and their co-occurrence with various neoflavanoids when considered in association with recent results[3] on the biosynthesis of the 4-arylcoumarin, calophyllolide, provides support for our hypothesis[1,2] of neoflavanoid formation.

Examination[†] of the natural products (I)—(VI) showed that they were 1,3-diarylpropenes with hydroxy- and methoxy-substituents. Their n.m.r. spectra showed the multiplets characteristic of an ABX_2 system with a coupling constant between the olefinic protons (J_{AB} *ca.* 16 c./sec.) which indicated a *trans*-disubstituted ethylenic double bond. Details of the chemical shifts and coupling constants for the $-CH_A{=}CH_B{-}CH_2-$ unit of similar synthetic *trans*-cinnamylphenols have previously been reported.[4] The structures of the natural products (I)—(VI) were proved by synthesis as outlined below. The synthetic cinnamylphenols (I) and (V) have previously been described[4] and were identical in all respects with obtusastyrene (I) and mucronustyrene (V). Obtustyrene (II), violastyrene (III), and isoviolastyrene (IV) were synthesised by the reduction of the corresponding chalcones ($\rangle C{=}O$ to $\rangle CH_2$) with an ethereal solution of lithium aluminium hydride in the presence of aluminium chloride. Since this

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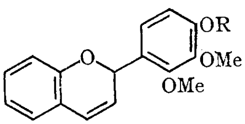
[†] All new natural products and intermediates associated with their synthesis have been fully characterised by analysis, spectroscopic (u.v., i.r., and n.m.r.) and mass spectrometric examination.

reduction may be accompanied by rearrangement of the double bond,[5] the structure of violastyrene (III) was rigorously proved. This was achieved by oxidative degradation (osmium tetroxide followed by sodium periodate) of violastyrene methyl ether, which gave 2,4,5-trimethoxyphenylacetaldehyde, and also by the synthesis of violastyrene (III) by the *para*-Claisen rearrangement of 1-cinnamyloxy-2,5-dimethoxybenzene. A low yield synthesis of violastyrene (III) by the reaction of 2,5-dimethoxyphenol with cinnamyl diphenyl phosphate[6] is of interest in relation to our biogenetic proposals.[1] The constitution of petrostyrene (VI) isolated from an, as yet, unidentified *Machaerium* species was settled by the reduction of 2,5′-diethoxy-2′,3′,4′-trimethoxychalcone with lithium aluminium hydride and aluminium chloride which yielded petrostyrene diethyl ether.



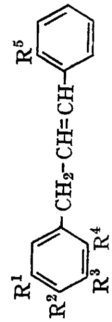
(X) R=H
(XI) $R=CH_2Ph$

Mucronulastyrene (VII), villostyrene (VIII), and kuhlmannistyrene (IX) had molecular formulae and spectroscopic properties consistent with cinnamylphenol structures with hydroxy- and methoxy-substituents, but the n.m.r. spectra associated with the $-CH_A{=}CH_B{-}CH_2-$ unit showed a vicinal coupling constant between the olefinic protons (ABX_2 system with J_{AB} 11—12 c./sec.), which indicated that the double bond had a *cis*- rather than a *trans*-configuration. The constitution of mucronulastyrene (VII) followed from the oxidative degradation of its diethyl ether, which by oxidation with osmium tetroxide followed by sodium periodate yielded 2-ethoxybenzaldehyde; oxidation with potassium permanganate gave 4-ethoxy-2,3-dimethoxyphenylacetic acid.

Proof of the constitution of mucronulastyrene (VII) by synthesis required the development of a new synthetic method suitable for the preparation of *cis*-cinnamylphenols. Reduction of the flav-3-ene (X) with lithium aluminium hydride and aluminium chloride gave mucronulastyrene (VII), and this proved that the ethylenic group in mucronulastyrene had *cis*-geometry.

The constitution of villostyrene (VIII) followed from (i) the identity of villostyrene monomethyl ether with mucronulastyrene dimethyl ether, (ii) the formation of 2-methoxybenzoic acid when villostyrene was oxidised with potassium permanganate, and (iii) a detailed study of the n.m.r. spectra of villostyrene and its derivatives. The

Compound[a]	Substituents					Geometry of disubstituted ethylene	Source	Co-occurring neoflavanoids
	R^1	R^2	R^3	R^4	R^5			
Obtusastyrene (I)	H	OH	H	H	H	*trans*	*D. obtusa* Lecomte	(*R*)-4-Methoxydalbergione, 3-(2,5-dihydroxy-4-methoxyphenyl)-3-phenyl-1-propene (obtusaquinol)
Obtustyrene (II)	H	OH	H	OMe	H	*trans*		
Violastyrene (III)	OMe	OH	H	OMe	H	*trans*	*D. miscolobium* Benth. [syn. *D. violacea* (Vogel) Malme]	(*S*)-4′-hydroxy-4-methoxydalbergione, 6-hydroxy-7-methoxy-4-phenylcoumarin
Isoviolastyrene (IV)	OH	OMe	H	OMe	H	*trans*		
Mucronustyrene (V)	H	OH	OMe	OMe	H	*trans*	*M. mucronulatum* Mart. ex Benth.	—
Petrostyrene (VI)	OH	OMe	OMe	OMe	OH	*trans*	*M.* species (URB/18)	—
Mucronulastyrene (VII)	H	OH	OMe	OMe	OH	*cis*	*M mucronulatum* and *M. villosum* Vogel	—
Villostyrene (VIII)	H	OH	OMe	OMe	OMe	*cis*		—
Kuhlmannistyrene (IX)	OH	OMe	OMe	OMe	OH	*cis*	*M. kuhlmannii* Hoehne	6-Hydroxy-7,8-dimethoxy-4-phenylcoumarin (kuhlmannin), 6-hydroxy-7,8-dimethoxy-4-phenylchrom-3-ene (kuhlmannene), *R*-3-(5-hydroxy-2,3,4-trimethoxyphenyl)-3-(4-hydroxyphenyl)-1-propene (kuhlmanniquinol)



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[a] All the cinnamylphenols were obtained as oils except violastyrene (III), m.p. 84—85°, and isoviolastyrene (IV), m.p. 86—88°.

constitution (VIII) was confirmed by the following synthesis. Reduction ($LiAlH_4$–$AlCl_3$) of the flav-3-ene (XI) gave the *cis*-cinnamyl phenol, [the 4-benzyl ether of (VII)], which by the consecutive methylation and debenzylation gave villostyrene (VIII).

The spectroscopic properties of kuhlmannistyrene (IX) indicated that it was the *cis*-isomer corresponding to the *trans*-cinnamylphenol, petrostyrene (VI). The constitution (IX) of kuhlmannistyrene was settled by showing that catalytic hydrogenation of kuhlmannistyrene (IX) and petrostyrene (VI) gave dihydro-derivatives which were identical.

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[1] W. B. Eyton, W. D. Ollis, M. Fineberg, O. R. Gottlieb, I. Salignac de Souza Guimarães, and M. Taveira Magalhães, *Tetrahedron*, 1965, **21**, 2697; W. D. Ollis, *Experientia*, 1966, **22**, 777; W. D. Ollis in "Recent Advances in Phytochemistry", ed. T. J. Mabry, R. E. Alston, and V. C. Runeckles, Appleton–Century–Crofts, New York, 1968, p. 328; W. D. Ollis and O. R. Gottlieb, *Chem. Comm.*, 1968, 1396.

[2] W. B. Eyton, W. D. Ollis, I. O. Sutherland, O. R. Gottlieb, M. Taveira Magalhães, and L. M. Jackman, *Tetrahedron*, 1965, **21**, 2683.

[3] G. Kunesch and J. Polonsky, *Chem. Comm.*, 1967, 317.

[4] M. F. Barnes, W. D. Ollis, I. O. Sutherland, O. R. Gottlieb, and M. Taveira Magalhães, *Tetrahedron*, 1965, **21**, 2707.

[5] P. N. Verma and M. M. Bokadia, *Chem. and Ind.*, 1964, 807.

[6] J. A. Miller and H. C. S. Wood, *Chem. Comm.*, 1965, 39.