The Synthesis of Cinnamyl Pyrophosphate and its Reaction with Resorcinol

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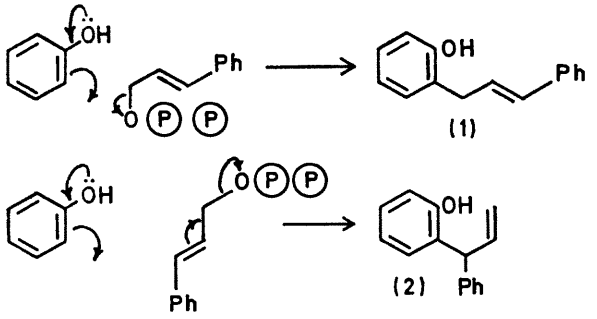
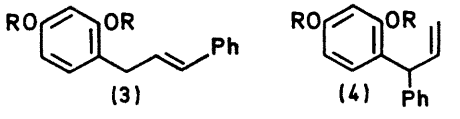
Summary Cinnamyl pyrophosphate has been prepared for the first time, and reacts with resorcinol to give a cinnamyl-phenol and a neoflavanoid consistent with Ollis' postulate for the biosynthesis of these compounds.

OLLIS has suggested[1] that the biosynthesis of cinnamyl-phenols and neoflavanoids, which frequently occur together



in Nature, involves cinnamylation of phenolic precursors with cinnamyl pyrosphosphate. Cinnamylation of the phenol can occur by an S_N2 or an S_N2' type pathway to give respectively cinnamyl-phenols (1) and neoflavanoids (2). Jurd has suggested[2] that protonated cinnamyl alcohol should show reactivity similar to that of cinnamyl pyrophosphate, and has described the reaction between cinnamyl alcohol and resorcinol in aqueous acetic acid from which he isolated the cinnamyl-phenol (3; R = H) and



obtained spectroscopic evidence for the presence of the neoflavanoid (4; R = H).

Cinnamyl pyrophosphate is an unknown compound which, hitherto, has never been synthesised nor isolated from natural sources. We have now achieved the synthesis as follows, and have studied the reactivity of the product.

Treatment of cinnamyl alcohol with phosphoric acid in trichloroacetonitrile in the presence of triethylamine according to Cramer's method[3] gave the monophosphate.

This was converted into the phosphoromorpholidate and subsequently into the pyrophosphate using the procedures devised by Khorana[4] for the preparation of nucleoside-5′-pyrophosphates. Cinnamyl pyrophosphate was purified by chromatography on DEAE cellulose, eluting with triethylammonium hydrogen carbonate solution. It was isolated as its cyclohexylammonium salt, as was the monophosphate. These salts were readily separable by paper chromatography and this was used as a criterion of purity. Their structures were established by elemental analysis, u.v. spectroscopy, and by hydrolysis with dilute acid to cinnamyl alcohol and either phosphate or pyrophosphate. Cinnamyl pyrophosphate was heated with resorcinol in aqueous ammonium acetate buffer, pH 7·2. The crude reaction product (*ca.* 10% conversion) was treated with dimethyl sulphate and alkali, and the principal products were identified as *trans*-3-(2,4-dimethoxyphenyl)-1-phenylpropene (**3**; R = Me) and 3-(2,4-dimethoxyphenyl)-3-phenylpropene (**4**; R = Me) in a ratio of 3 : 1. These two compounds, in the same proportions, were obtained when, following the work of Jurd,[2] we re-examined the reaction of cinnamyl alcohol with resorcinol in aqueous acetic acid, and methylated the crude reaction product. We have established, however, that cinnamyl pyrophosphate is not hydrolysed to cinnamyl alcohol on heating in aqueous buffer of pH 7·2. The methylated products were isolated by preparative g.l.c., and their structures assigned on the basis of i.r., n.m.r., and mass spectroscopy.

These results establish beyond all doubt the chemical feasibility of Ollis' theory of biogenetic *C*-alkylation with cinnamyl pyrophosphate leading to the formation of cinnamyl-phenols and neoflavanoids.

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