# Stereochemistry of the Decarboxylation of Phenolic Cinnamic Acids by *Saccharomyces cerevisiae*

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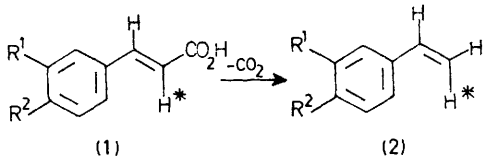
*Summary* The decarboxylation of (*E*)-3,4-dimethoxycinnamic acid to the corresponding styrene by *S. cerevisiae* proceeds with retention of the hydrogen atom at the α-position of the acid; the configuration of the double bond is also retained.

ALTHOUGH the non-oxidative decarboxylation of phenolic cinnamic acids [*e.g.* *p*-coumaric (**1a**), ferulic (**1b**), and caffeic (**1c**) acids] to the corresponding styrenes (**2**) occurs widely in bacteria[1,2] and in yeast,[1,3] the enzymic mechanism is unknown. As a preliminary approach to its clarification, the stereochemical course of the reaction has been investigated. We now report that the decarboxylation of 3,4-dimethoxycinnamic acid (**1d**) by a strain of *Saccharomyces cerevisiae*† results in retention of configuration at the side-chain double bond (Scheme).

A culture medium‡ containing a suspension of (*E*)-3,4-dimethoxy[α-$^2$H]cinnamic acid (**1d**, H* = $^2$H) (D atoms per molecule 0·80 ± 0·03 by m.s.)[4] was inoculated with yeast and shaken at 25° for 24 h. The ether extract of the fermentation medium, when evaporated and chromatographed on silica gel [light petroleum (b.p. 40—70°)–benzene 1:1], gave (*Z*)-3,4-dimethoxy[β-$^2$H]styrene (**2d**, H* = $^2$H)[5] (62% yield; D atoms per molecule 0·75 ± 0·03




(1) (2)

(a); $R^1$ = H, $R^2$ = OH
(b); $R^1$ = OMe, $R^2$ = OH
(c); $R^1$ = OH, $R^2$ = OH
(d); $R^1$ = OMe, $R^2$ = OMe

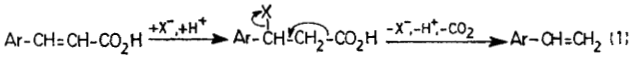
SCHEME

† This strain (28 C)[3] is unique in decarboxylating both 3,4-dimethoxycinnamic acid and ferulic acid. Its use made our investigation easier, 3,4-dimethoxystyrene being more stable than 4-hydroxystyrenes.

‡ Glucose (100 g), yeast nitrogen base (Difco) (7 g), $NaH_2PO_4$ (13 g), water (1 l).

by m.s.). The position of the deuterium atom was assigned by comparison of the $^1H$ n.m.r. spectrum (vinyl group region) of (**2d**) with the spectral patterns calculated for each of the three 3,4-dimethoxystyrenes monodeuteriated in their side-chain. The calculations, (using the second-order perturbation method), were based on the chemical shifts and spin-coupling constants of the vinyl protons of 3,4-dimethoxystyrene ($\delta_A$ 5·56, $\delta_B$ 5·12, $\delta_X$ 6·66 p.p.m.; $J_{AX}$ 17·5, $J_{BX}$ 10·6, $J_{AB}$ 1·4 Hz in $CDCl_3$) and assumed (a) that $J_{HD} = (\gamma_D/\gamma_H)J_{HH}$ and (b) that the chemical shifts are not affected by deuterium substitution.[6] The correctness of these assumptions was confirmed by comparing the observed and theoretical spectrum of (*E*)-3,4-dimethoxy-[$\beta$-$^2$H]styrene prepared by unequivocal synthesis *via* $D_2O$ decomposition of the Grignard reagent[6] of *trans*-3,4-dimethoxy-$\beta$-bromostyrene.[7]

If the hypothesis is made that the *in vivo* decarboxylation of cinnamic acids takes place similarly to the *in vitro* pyridine or thioacetic acid-catalysed decarboxylation of benzylidenemalonic acid derivatives,[8] *i.e.* by a 1,2-addition, 1,2-elimination mechanism (equation 1), then a *cis*-addition followed by a *trans*-decarboxylative elimination (or a *trans*-addition and *cis*-elimination) must be assumed to account for the overall stereochemistry of the process.



(1)

($X^-$ = nucleophilic group of the enzyme, *e.g.* $RS^-$, $RO^-$)

It is also remarkable that (*Z*)-3,4-dimethoxycinnamic acid[9] does not undergo decarboxylation by the above strain of *S. cerevisiae*.

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