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Regioselective Dimerization of Ferulic Acid in a Micellar Solution

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Introduction. Hydroxycinnamates have been recognized as important components of plant cell walls (1). Ferulic acid dehydromers are able to cross-link different polysaccharide chains and, in some cases, polysaccharide and lignin (2). Cross-linking of cell wall components is expected to have a marked influence on numerous cell wall properties such as accessibility, extensibility, plasticity, digestibility, and adherence (3). Different kinds of ferulic acid dehydromers have been identified in plant materials, with the 8–O–4-dehydromer often being the most abundant (4). In contrast, the primary ferulic acid dehydromer generated *in vitro* from ferulic acid esters is the 8–5-coupled product, **4**, when utilizing the biomimetic peroxidase–hydrogen peroxide system (5) or a range of single-electron oxidants (4,5). Obviously, some kind of control must be utilized in the cell in order to produce regioselective dehydromers.

Aim. To investigate whether oxidative coupling of *trans*-ferulic acid can be regioselectively controlled using surfactants.

Results and discussion

It is known that photodimerization of cinnamic acids can be controlled by the action of quaternary ammonium or amine *N*-oxide surfactants (6). These surfactants may form micelles in aqueous solutions with the ionic part at the surface to the water. Carboxylic acids will be organized around them with the acid part pointing inwards. With *trans*-ferulic acid and a strongly basic surfactant a similar organization is expected to happen as the stronger acid moiety (K_a of carboxylic acid $\gg K_a$ of phenol) will be orientated towards the aggregates (Figure 1). With an acidic surfactant this orientation is still expected as the undissociated carboxylic acid moiety will have a greater polarity compared to a phenolic group.

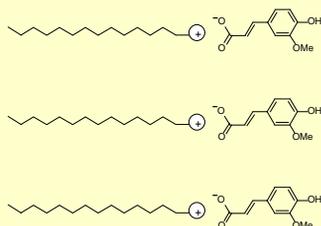


Figure 1. Orientation of ferulic acid in a micellar solution.

In the presence of H_2O_2 and peroxidase, we have found that the combination of *trans*-ferulic acid and the strongly basic surfactant hexadecyltrimethylammonium hydroxide in a molar ratio of 1:1 gave a complete reaction within 5 min. The distribution of products was quantified by analytical HPLC and were 25% **2**, 21% **3**, and 14% **4** (Figure 2). During the reaction, the pH of the solution changed from 7.0 to 8.0. Repeating this experiment in a buffered solution (pH 7.5) but without surfactant gave a different product distribution as no **3** was produced. The major products were **2** and **4**. Unidentified polymeric or higher oxidized products accounted for the remainder in both the micellar and buffered solutions as an almost complete conversion of *trans*-ferulic acid was observed. With *p*-coumaric and sinapic acid as substrates a similar but more complex reaction pattern were observed. Changing the surfactant to tetradecyltrimethylammonium bromide gave 18% **5** and only small amounts of **2** and **4** (Figure 2) but with a substantial amount of polymeric or higher oxidized compounds. The pH remained constant at 3.0 during the reaction. Repeating this experiment in a buffered solution (pH 3.0) but without surfactant gave no reaction. A molar excess of surfactant (50–100 %) to *trans*-ferulic acid gave the cleanest reactions.

Compound **5** closely resembles the lignan pinosresinol, which has recently been stereoselectively prepared from coniferyl alcohol by means of a "guiding" protein (7)

With other substrates, *p*-coumaric or sinapic acid, only trace amount of dimer products were observed.

In general for all the reactions mentioned, the absence of peroxidase or H_2O_2 gave no reaction and the amount of peroxidase and reaction time could be increased 10 times without changing the product distribution and yield.

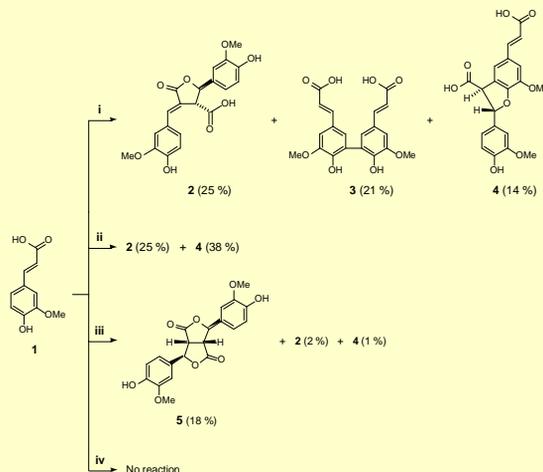


Figure 2. Dimerization of *trans*-ferulic acid in a micellar solution with hexadecyltrimethylammonium hydroxide and tetradecyltrimethylammonium bromide as the surfactant, respectively, and the corresponding dimerizations in non-micellar buffered solutions. Reaction time: 5 min. (i) Ferulic acid/hexadecyltrimethylammonium hydroxide (1:1), peroxidase, H_2O_2 (pH 7.0–8.0). (ii) Peroxidase, H_2O_2 , 0.1 M acetate buffer solution (pH 7.5). (iii) Ferulic acid/tetradecyltrimethylammonium bromide (1:2), peroxidase, H_2O_2 (pH 3.0). (iv) Peroxidase, H_2O_2 , 0.1 M phosphate buffer solution (pH 3.0) (8).

Conclusion

From the present results it can be concluded that the outcome of radical dimerization of hydroxycinnamic acids is dependent on both the geometric and electronic nature of a controlling agent, and seems to offer a new way to produce dehydromers of hydroxycinnamic acids on a preparative scale. Although micelles might not be involved in the biosynthetic assembly of these dehydromers, the present results indicate that a controlling agent might be present *in vivo*, e.g. "guiding" proteins as in the case of the biosynthesis of lignins and lignans.

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