

Synthesis of *p*-Hydroxycinnamyl-*p*-Coumarate and Ferulate Mono- and Diglucosides

F.H. Ludley and J. Ralph

Introduction

Grass lignins have substantial amounts of *p*-coumaric acid esterified, as we have recently shown (see last year's Summaries), specifically at the γ -position of lignin sidechains. This implicates the incorporation of the *p*-coumarate esters of the lignin monomers coniferyl and sinapyl alcohols in the lignin biosynthesis. However, our attempts to prepare synthetic lignins mirroring the structure of the native grass lignins have been hampered by the extreme aqueous insolubility of these esterified compounds. We reasoned that glucoside derivatives should be much more soluble, can release the esterified monomers when glucosidase enzymes are used, and may even mimic the manner in which the plant transports these compounds to the cell wall for their subsequent polymerization. Of course, synthesis of the required glucosides was far from a trivial task. One puzzling feature of grass lignins that we hope to answer using these compounds is why the *p*-coumarate unit does not become involved in the free-radical reactions of lignification; under in vitro conditions with model compounds, the *p*-coumarate enters freely into these coupling reactions.

Method

Reaction of the *p*-hydroxybenzaldehydes **1a,b** with 2,3,4,6-tetra-*O*-acetylglucopyranosylbromide **2** and potassium carbonate in acetone at room temperature gives the *p*-hydroxybenzaldehyde-2,3,4,6-tetra-*O*-acetyl-glucopyranosides **3a,b**. The compounds precipitate cleanly from a toluene/petroleum ether solution and no further recrystallization is necessary. Knoevenagel-condensation of **3a,b** with malonic acid in pyridine/piperidine at 100°C leads to the *p*-hydroxycinnamic acid-2,3,4,6-tetra-*O*-acetyl-glucopyranosides **4a,b**. Reacting *p*-hydroxycinnamaldehydes **5a,b** with 2,3,4,6-tetra-*O*-acetyl-glucopyranosylbromide **2** under the conditions mentioned above yields the glucosides **6a,b** which are reduced in very high yields to the *p*-hydroxycinnamylalcohol-2,3,4,6-tetra-*O*-acetylglucopyranosides **7a,b**. All acetyl-protecting groups remain intact during this reaction; no

further work-up of the products is needed. Condensation of **4a,b** with **7a,b** proceeds at room temperature in methylene chloride using dicyclohexylcarbodiimide (DCC) and 4-*N,N*-dimethylaminopyridine (DMAP) as catalysts and gives the final products (esters) **8a-c** in yields between 53.4 and 80.6%. The products are isolated again by precipitation out of toluene/petroleum ether, purified by column chromatography and recrystallized from 95% ethanol. All compounds were characterized directly by NMR-spectroscopy. To enhance the solubility in water necessary for the following preparations of DHP's, the acetate protecting groups are cleaved using either a solution of pyrrolidine in 95% ethanol or sodium bicarbonate in methanol. The latter method is sometimes disadvantageous because some of the compounds undergo an ester cleavage during the deacetylation reaction. Nevertheless, it is a surprise that such a mild reagent as sodium bicarbonate is capable of not only cleaving phenolic acetates but also aliphatic ones. It is even more interesting that it cleaves the ester bond in some of the compounds **8a-c** proving, on the other hand, that these bonds are relatively weak compared to other ester bonds. To remove any residues of acetylated material, the compounds were washed once with acetone and dried. Yields of the final compounds **9a-c** prepared during these reactions are between 83 and 98%.

The main purpose of preparing the *p*-hydroxycinnamyl *p*-coumarates and ferulates as diglucosides **9a-c** was to increase their water solubility compared to the free phenolic structures. To investigate whether the water solubility would already be high enough with only one glucoside attached, the *p*-hydroxycinnamyl *p*-coumarate and ferulate monoglucosides **12a-c** were prepared using an analogous reaction sequence.

Discussion and Conclusion

A synthetic method has been developed to prepare *p*-hydroxycinnamyl *p*-coumarate and ferulate mono and diglucopyranosides. An advantage of the reaction sequence shown is that most of the precu-

sors and intermediate compounds can be easily isolated by precipitation from toluene/petroleum ether solutions and need no further purification. The preparation of the esters **9a-c**, as well as the deacetylation reactions leading to the final prod-

ucts **12a-c**, gives good yields. We shall now utilize these compounds to make synthetic lignins to mimic grass lignins and to explore why the *p*-coumarate group does not become involved in the radical coupling lignification reactions.

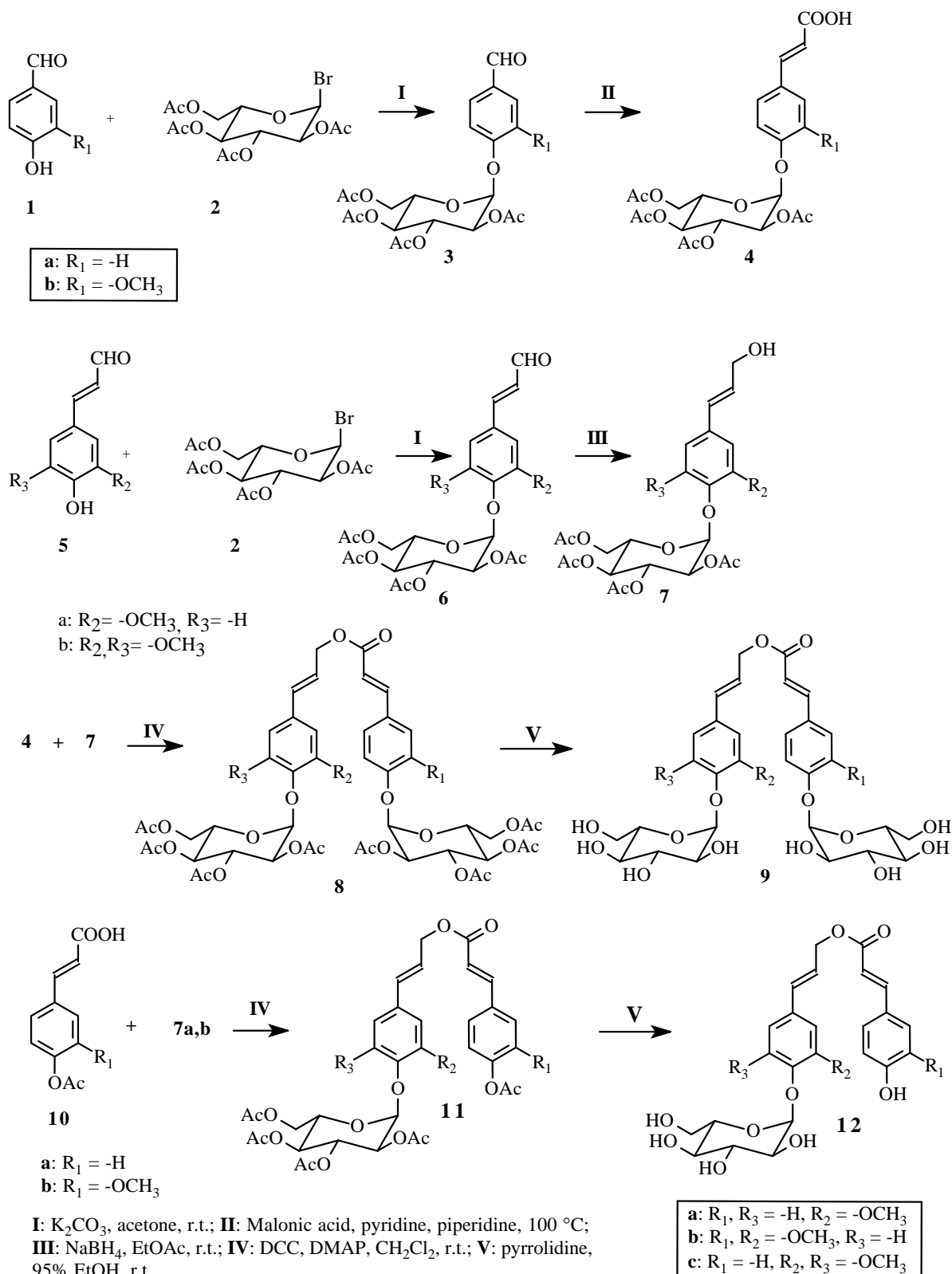


Figure 1. Synthetic scheme used to prepare hydroxycinnamyl *p*-hydroxycinnamate derivatives.