

## Short Research Article

# Deuteration of dietary antioxidants: ferulic acid derivatives and $\alpha$ -tocopherol<sup>†</sup>

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Received 29 June 2006; Revised 22 November 2006; Accepted 23 November 2006

**Keywords:** deuterium labeling; ferulic acid;  $\alpha$ -tocopherol

## Introduction

The potential health benefits of ferulic acid and other hydroxycinnamates have raised interest in recent years. These phenolic acids can be found in the human diet, e.g. in cereal brans.<sup>1</sup> Ferulic acid has been reported to have biological activities such as antioxidant, antimicrobial, anti-inflammatory, antithrombotic and anticancer properties. Investigation of the antioxidant properties have shown ferulic acid to have high scavenging activity for hydrogen peroxide, superoxide, hydroxyl radical and other oxidative species.<sup>2</sup>

Another dietary antioxidant is  $\alpha$ -tocopherol which belongs to the vitamin E family. Tocopherols are present in oil seeds, leaves and other green parts of higher plants. Vitamin E is the most important fat-soluble antioxidant having various beneficial effects including protection against cancer, cardiovascular diseases, free radical induced damage on cell membrane and DNA and oxidation of low density lipoproteins.<sup>3</sup>

We have sought a simple and efficient synthesis for the deuterated ferulic acid derivatives **1–3** and  $\alpha$ -tocopherol **4**. Stable and pure deuterated analogues are required for the development of quantitative analysis and for metabolic studies.

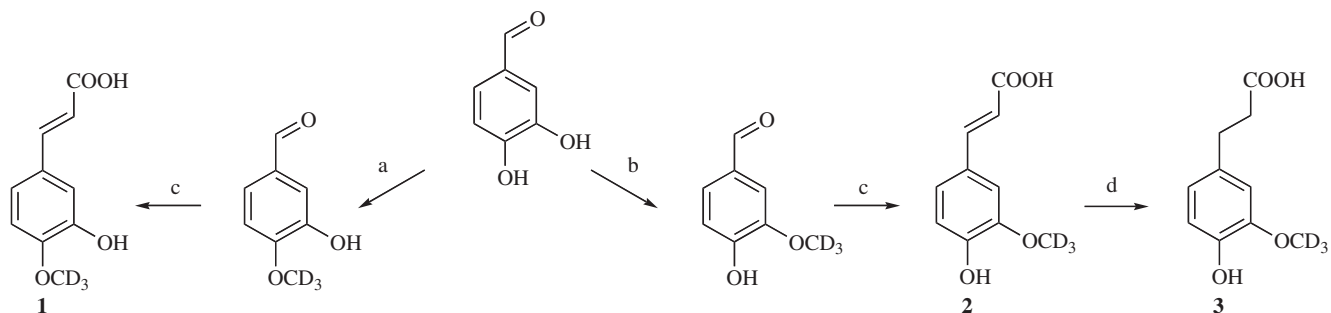
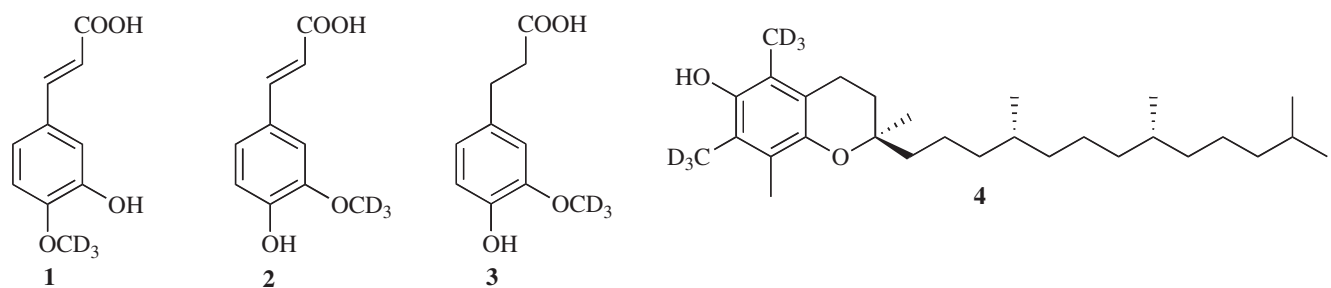
## Results and Discussion

Deuterated ferulic acids were prepared starting from 3,4-dihydroxybenzaldehyde which was selectively methylated with CD<sub>3</sub>I. Products were either [D<sub>3</sub>]vanillin or [D<sub>3</sub>]isovanillin depending on the base and solvent used in the reaction and the reaction time. These intermediates were alkylated by the Doebner modification of Knoevenagel condensation under microwave irradiation giving both ferulic acids in good yield (Scheme 1).

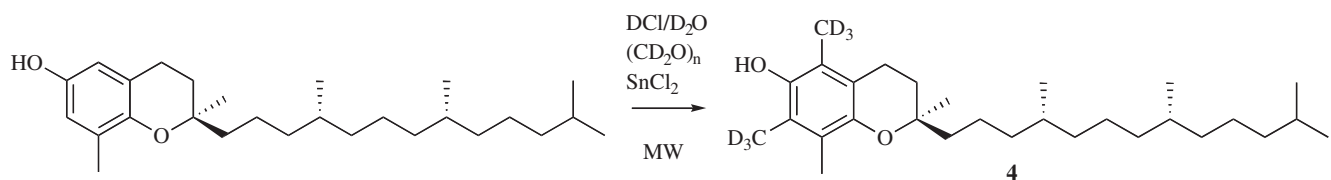
For deuterated  $\alpha$ -tocopherol, we applied microwave enhancement of the synthesis starting from  $\delta$ -tocopherol<sup>4</sup> (Scheme 2). Reaction time was shortened from 4 hours to less than half an hour and reduced amounts of reagents were needed.

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<sup>†</sup>Proceedings of the Ninth International Symposium on the Synthesis and Applications of Isotopically Labelled Compounds, Edinburgh, 16–20 July 2006.



Scheme 1



Scheme 2

In conclusion, we have developed efficient synthesis of deuterium labelled ferulic acid derivatives by selective methylation of vanillin and isovanillin. Microwave irradiation was found to be practical in the preparation of  $[D_6]\alpha$ -tocopherol.

## REFERENCES

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