3-Step Synthesis of Caffeic Acid Phenethyl Ester

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Independent Project Abstract

3-Step Synthesis of CAPE

Caffeic Acid Phenethyl Ester (CAPE) is the active polyphenol of propolis, a resin-like material that acts as a natural sealant in honeybee hives. Studies suggest that CAPE has notable human health benefits, for it inhibits the activity of 5-lipoxygenase (5-LO)—a key enzyme in the metabolism of arachidonic acid (AA) to leukotriene A4 (LTA4)—and thus hinders the development of a variety of diseases such as inflammatory bowel disease, atherosclerosis, and asthma. Although CAPE can be found in nature, it may not be readily available; mastering its synthesis in the laboratory setting renders it available for wider human use. The proposed three-step synthesis of CAPE demonstrates the utilization of protecting groups in ether formation. Caffeic acid is acetylated with acetic anhydride in step one. The resulting intermediate is converted to a readily reactive acid (carboxylic) chloride by treatment with a Vilsmeier-Haack intermediate under dimethylformamide (DMF) activation. Step two then continues with alcoholysis, as the acid chloride intermediate and 2-phenylethanol are allowed to react—producing the acetylated ester intermediate form of CAPE. In the final step, base-induced de-O-acetylation with potassium carbonate in methanol and dichloromethane removes the acetyl protecting groups and reinstalls alcohol. In attempt to make this synthesis more green, highly reactive and hazardous acetic anhydride is replaced with a combination of glacial acetic acid (ethanoic acid) and zinc dust for acetylation in step one. If the proposed green step is successful, an alternative manner for installing protective groups will be achieved. Factors of cost, efficiency, reaction rate, and time must be further considered before accepting the proposed synthesis as a beneficial green alternative to traditional methods.