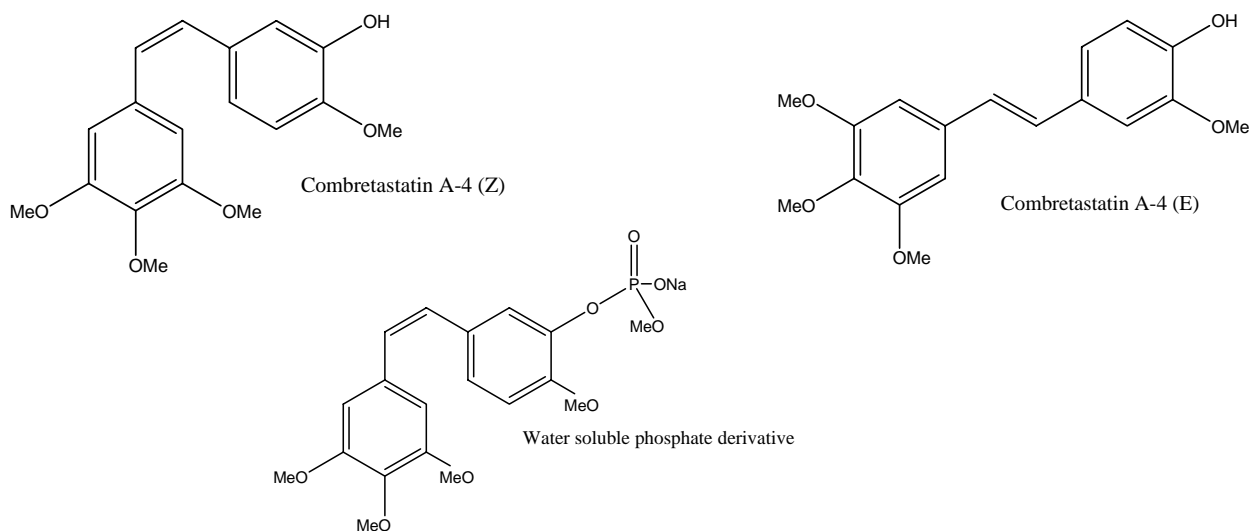


## “Novel Syntheses of Cis and Trans Isomers of Combretastatin A-4”

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Combretastatin A-4 is a potent cytotoxic agent that can be isolated from the bark of the South African tree *Combretum caffrum*. Combretastatin A-4 is capable of causing irreversible vascular shutdown within tumors while leaving normal vasculature intact. Currently, the water soluble phosphate derivative of combretastatin A-4 is in phase II of clinical trials. Presently a five-step Wittig synthesis is used to produce combretastatin A-4 non-stereoselectively; however, the (Z) stereoisomer is more active and is therefore desired. A two-step, stereoselective synthesis has been developed to produce the (Z) stereoisomer in high yield via Perkin condensation of 3,4,5-trimethoxyphenylacetic acid and 3-hydroxy-4-methoxybenzaldehyde followed by decarboxylation of the cinnamic acid intermediate. The conversion from the (Z) isomer to the (E) isomer is completed through iodine-catalyzed isomerization. The Suzuki cross-coupling of an aryl boronic acid and vinyl bromide is also successful in producing both (Z) and (E) isomers of combretastatin A-4.



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