Studies Towards the Asymmetric Total Synthesis of Ginkgolide B

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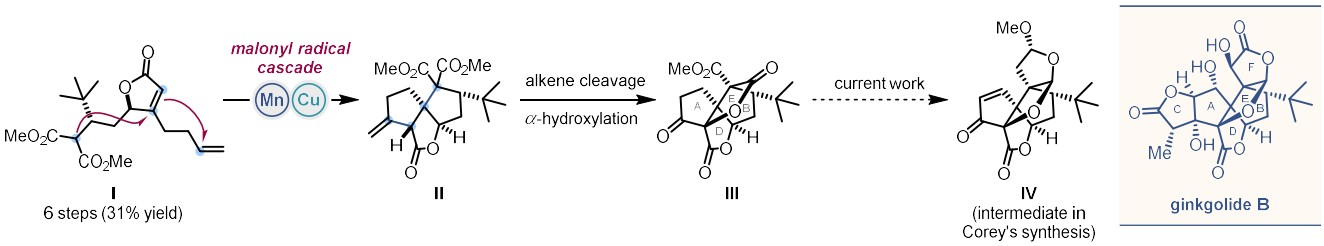
Ginkgolide B is a highly oxygenated diterpene with interesting neuroprotective properties. It is a potent platelet-activating factor (PAF) receptor antagonist that has shown potential for the treatment of Alzheimer's disease, dementia, and ischemia.[1] It contains a rare *tert*-butyl group, six heavily functionalised five-membered rings (A–F), and 11 chiral centres. Its complexity and therapeutic properties make ginkgolide B an attractive target for total synthesis, which has so far been achieved by Corey in 1988[2–4] and Crimmins in 2000.[5] Further to these, Barriault recently completed a racemic formal synthesis.[6]

Our approach towards ginkgolide B is based on a malonyl radical cascade; this enabled the synthesis of tricycle **II** from butenolide **I** with excellent diastereoselectivity. A two-step sequence involving alkene cleavage and α-hydroxylation was then used to construct ring E and deliver ginkgolide B's core (**III**). Current work is focused on the conversion of tetracycle **III** into pentacycle **IV**, an intermediate in Corey's total synthesis.[2–4] We envisage building ring F through decarboxylation, enolate alkylation, and directed reduction. This presentation will cover the synthesis and radical cascade of butenolide **I**, our efforts towards pentacycle **IV**, and the enantioselective organocatalysed reaction developed for the asymmetric route.



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