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Enantioselective Synthesis of Tatanans A–C and Reinvestigation of Their Glucokinase-Activating Properties
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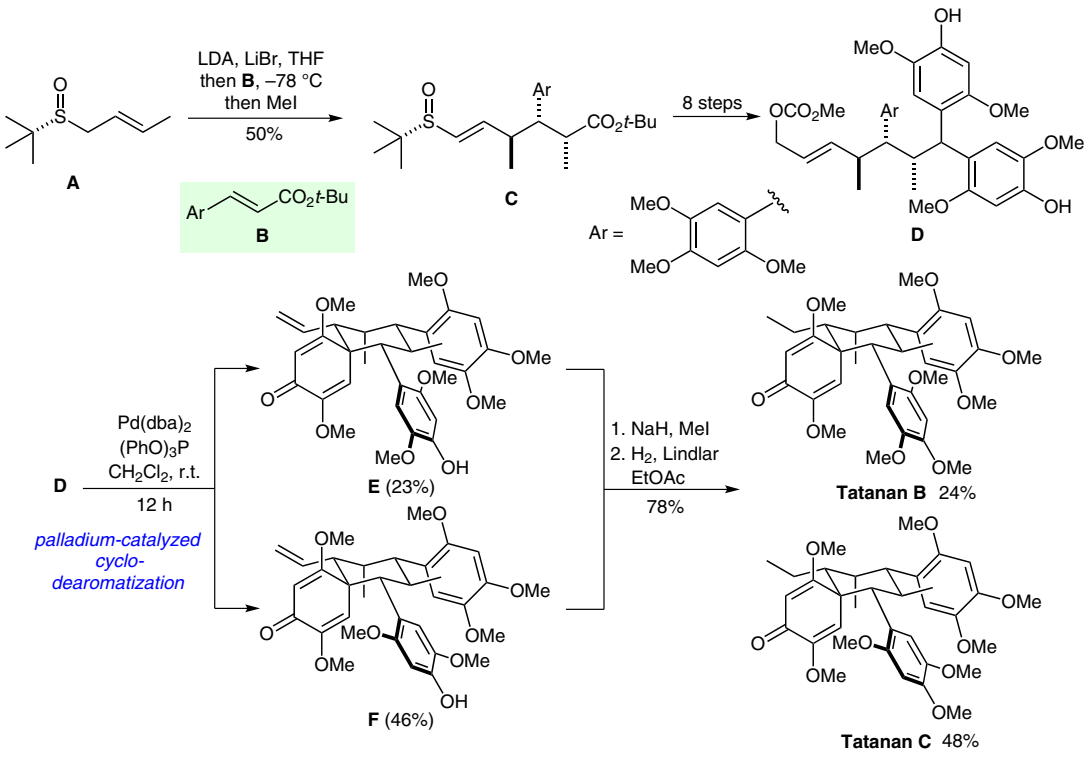
Synthesis of Tatanans A–C and Their Glucokinase-Activating Properties



Significance: The tatanans are sesquilignan natural products that have been reported to be powerful glucokinase activators, and thus potential antidiabetic agents (G. Ni et al. *J. Org. Chem.* **2011**, *76*, 2056). A. Zakarian, B. G. Miller and coworkers now report the first total syntheses of tatanans A–C and the re-evaluation of their biological activities. In contrast to the previous studies, however, they found that tatanans do not have any glucokinase-activating capabilities.

Comment: The synthesis of tatanans B and C commenced with a stereocontrolled conjugate addition–enolate trapping sequence that afforded **C**. Cleavage of the stereodirecting group was followed by addition of the aryl groups and further elaboration to afford allylic carbonate **D**. This underwent a remarkably selective palladium-catalyzed cyclodearomatization to give atropisomers **E** and **F** in 23 and 46% yield, respectively, along with another isomer in 15% yield (not shown). **E** and **F** could then be converted into the natural products by methylation and hydrogenation. The authors also accomplished the synthesis of tatanan A (not shown), an acyclic member of the family of natural products, by a sequence of Claisen rearrangements.

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Synthesis of Natural Products and Potential Drugs

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tatanans
[3,3]-sigmatropic rearrangements
cyclode-aromatization
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