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Total Synthesis of (+)-Linoxepin by Utilizing the Catellani Reaction
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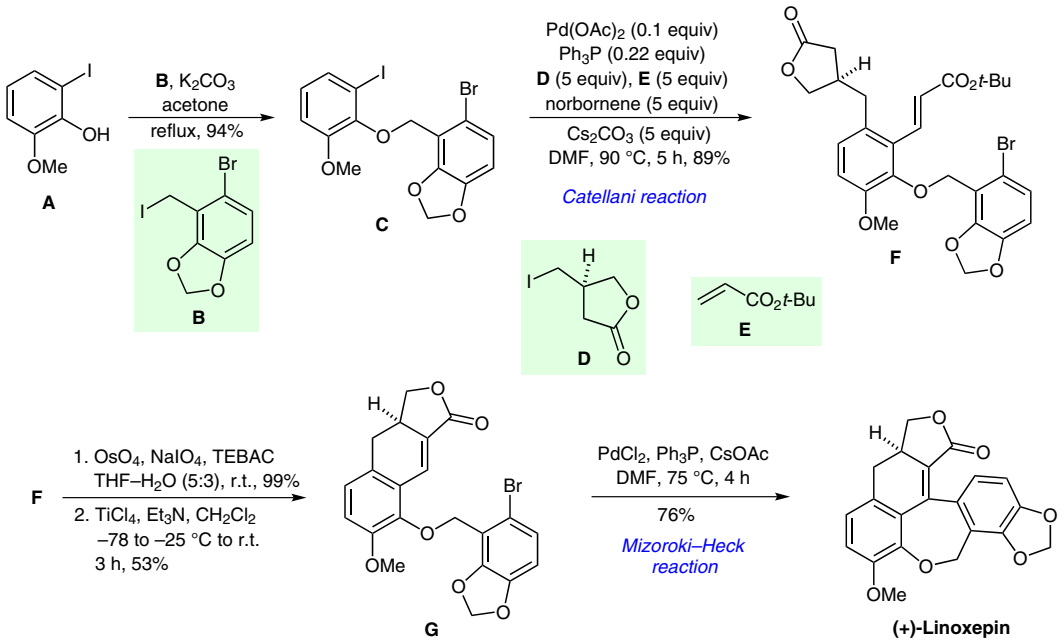
Total Synthesis of Linoxepin



Significance: Lautens and co-workers report the synthesis of linoxepin, a lignin isolated from *Linum perennne L.* (Linaceae). The elegant strategy relies on the Catellani reaction, in which a strained olefin (norbornene) is used to couple an iodoarene, an alkyl halide, and a terminal olefin using palladium catalysis. This is the first application of the Catellani reaction in the synthesis of a natural product and underscores the power of processes that form multiple bonds in a single step. In this context, it is worth highlighting the recent synthesis of linoxepin by Tietze and co-workers (*Angew. Chem. Int. Ed.* **2013**, *52*, 3191), which relies on a different palladium-catalyzed domino reaction.

Comment: Alkylation of phenol **A** with benzyl iodide **B** gave Catellani precursor **C** in 94% yield. The norbornene-mediated domino process involving aryl iodide **C**, enantiopure alkyl iodide **D** and acrylate **E** delivered key intermediate **F** in 89% yield. Oxidative cleavage of the olefin followed by $TiCl_4$-promoted aldol condensation furnished **G**, which in the presence of catalytic amounts of a palladium catalyst underwent a Mizoroki–Heck reaction to give (+)-linoxepin in 76% yield.

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