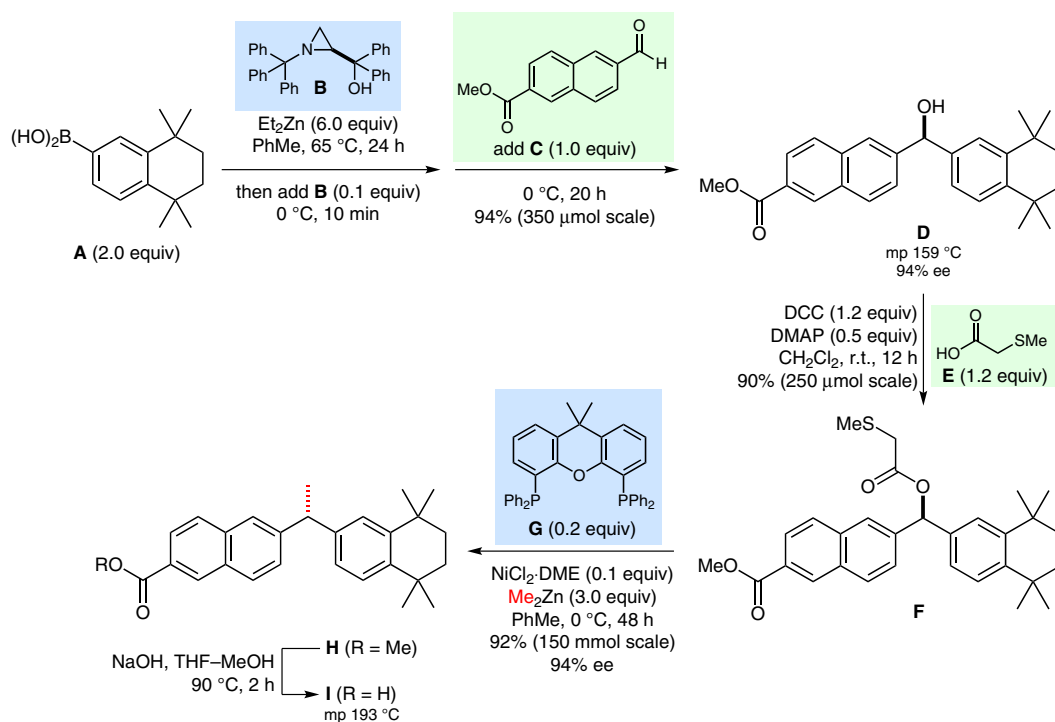


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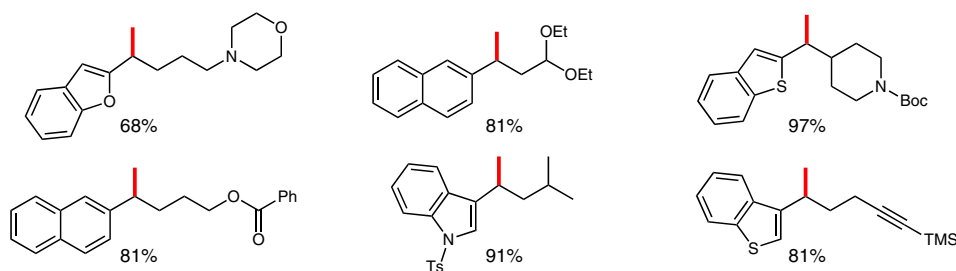
Functional-Group-Tolerant, Nickel-Catalyzed Cross-Coupling Reaction for Enantioselective Construction of Tertiary Methyl-Bearing Stereoisomers

J. Am. Chem. Soc. **2013**, *135*, 9083–9090.

Synthesis of a Retinoic Acid Receptor Agonist



Scope of the Negishi alkyl-alkyl cross-coupling



Significance: The target molecule **I** is a retinoic acid receptor γ (RAR γ) agonist that is of interest for the treatment of acne, psoriasis and melanoma. The synthesis depicted features the first nickel-catalyzed stereospecific Negishi alkyl-alkyl cross-coupling reaction of secondary benzylic α -(methylthio)acetate esters with dimethylzinc.

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Comment: The mild reaction conditions are compatible with a variety of functional groups including alkenes, protected alkynes, acetals, and esters. Heterocycles, amines, and imides are also well tolerated. Cross-coupling with diethylzinc is also possible but the reaction is more complex owing to additional competitive reaction pathways.