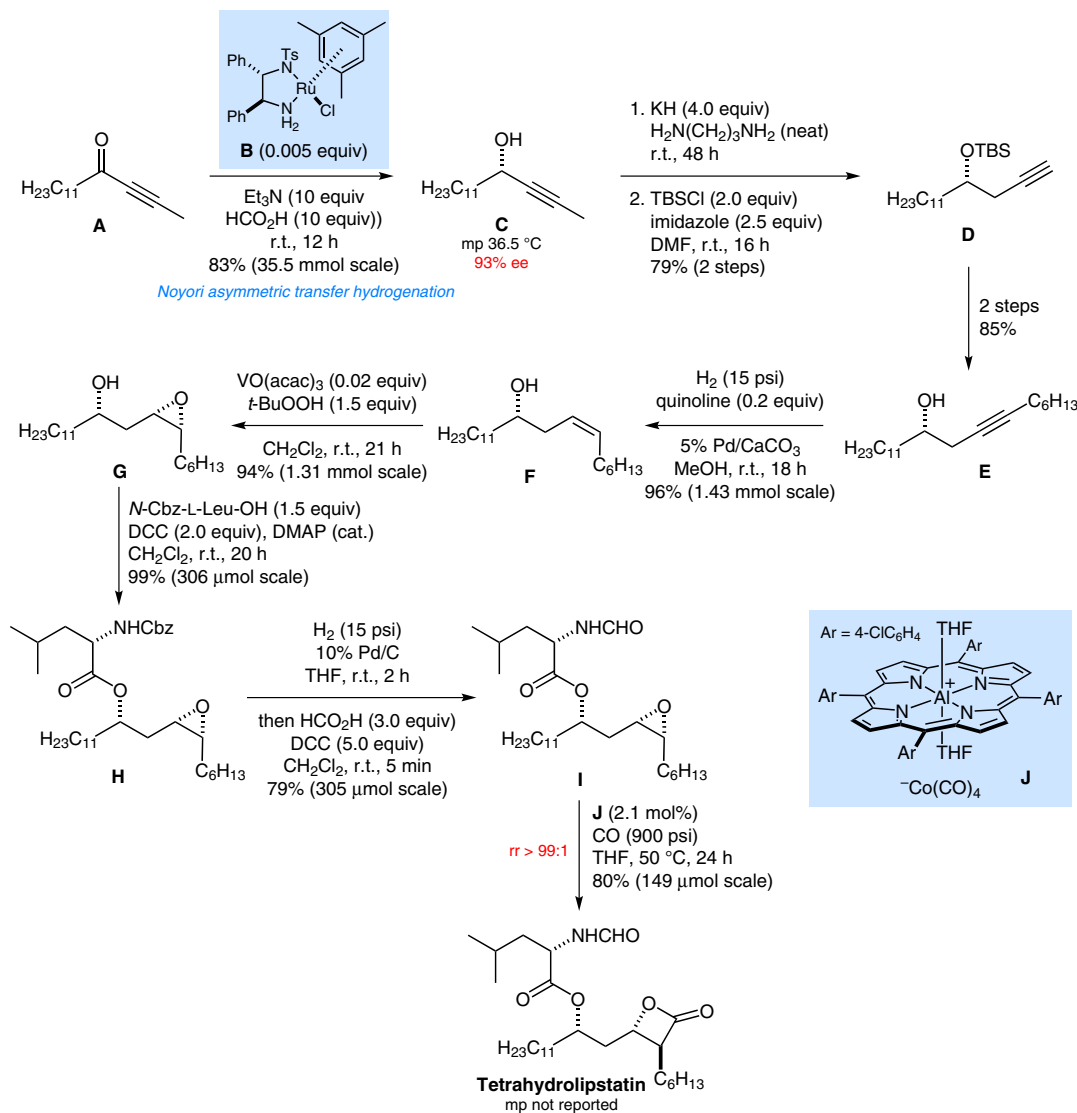


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 Total Synthesis of Tetrahydrolipstatin and Stereoisomers via a Highly Regio- and Diastereoselective Carbonylation of Epoxyhomoallylic Alcohols
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Synthesis of Tetrahydrolipstatin



Significance: Tetrahydrolipstatin (Xenical[®]) is a pancreatic lipase inhibitor that is marketed as a treatment for obesity. The eleven-step small-scale synthesis depicted (31% overall yield) features the regioselective carbonylation of the *cis*-epoxide **I** using the bimetallic [Lewis acid]⁺[Co(CO)₄]⁻ catalyst **J** to give the *trans*-β-lactone.

Comment: Seven diastereoisomers of tetrahydrolipstatin were also prepared by this epoxide carbonylation route. Attempts to synthesize epoxide **I** via the direct DCC coupling of *N*-formyl-L-leucine with **G** occurred with appreciable amounts of epimerization.

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