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Regio- and Enantioselective Palladium-Catalyzed Allylic Alkylation of Nitromethane with Monosubstituted Allyl Substrates: Synthesis of (*R*)-Rolipram and (*R*)-Baclofen
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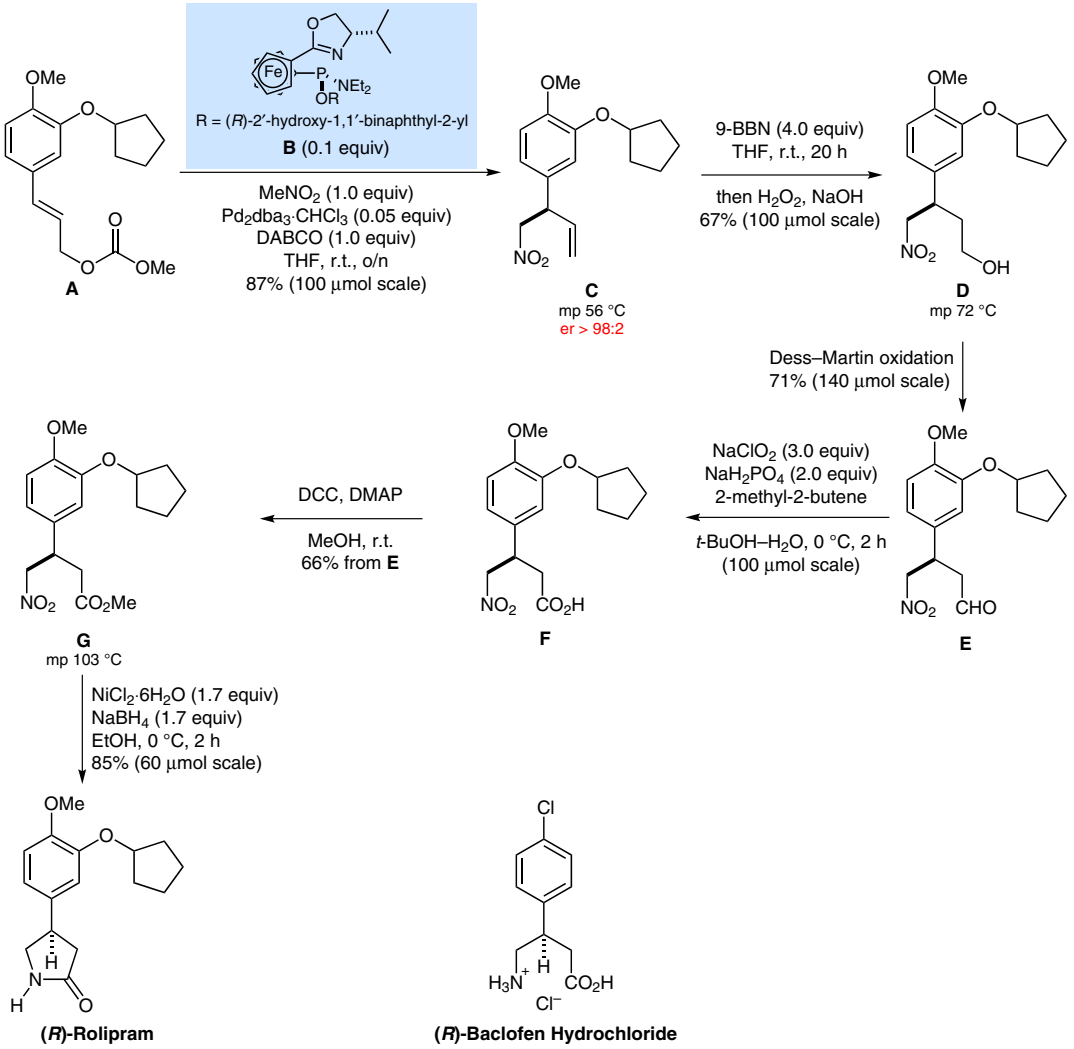
Category

Synthesis of Natural Products and Potential Drugs

Key words

(*R*)-rolipram
(*R*)-baclofen
asymmetric allylic alkylation
nitromethane
allyl carbonates
palladium

Synthesis of (*R*)-Rolipram



Significance: Rolipram is a phosphodiesterase-4 (PDE-4) inhibitor that displays potentially useful anti-inflammatory, antidepressant and antipsychotic effects. The key step in the micro-scale synthesis depicted is the palladium-catalyzed asymmetric allylic alkylation of nitromethane with the allylic carbonate **A**. High regio- and enantioselectivities were observed using the ferrocene-based SIOCPhox chiral ligand **B**.

Comment: The scope of the asymmetric allylic alkylation of nitromethane was explored using eleven aryl-substituted allyl methyl carbonates giving yields of 80–92% (one exception) and enantiomeric excesses of 90–98%. The reaction was also applied to an asymmetric synthesis of the anti-spasmodic agent (*R*)-baclofen.

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