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


**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.

**SYNFACTS Contributors:** Philip Kocienski

**Synfacts 2013, 9(1), 0011 Published online: 17.12.2012**

**DOI:** 10.1055/s-0032-1317720; **Reg-No.:** K09312SF