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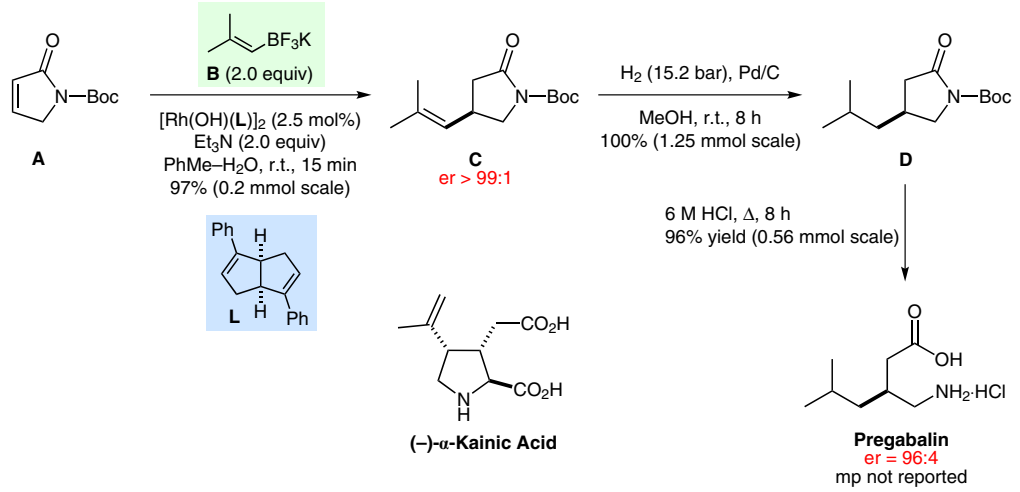
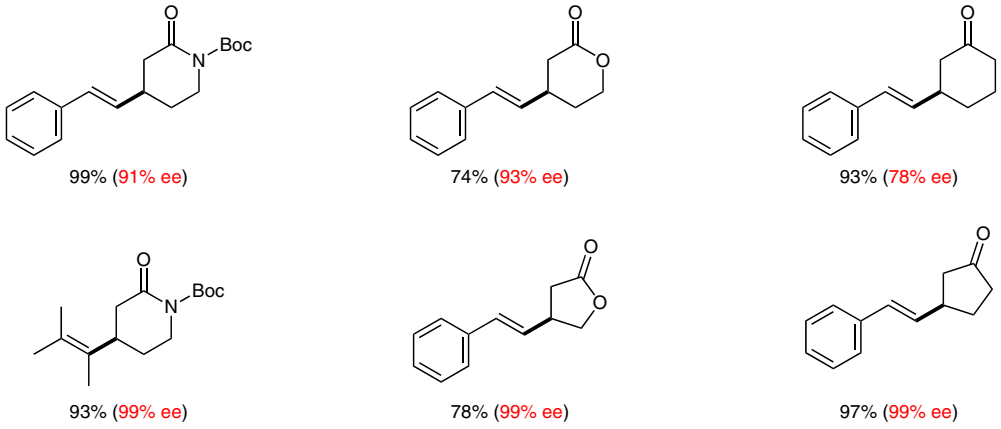
Highly Enantioselective Alkenylation of Cyclic α,β-Unsaturated Carbonyl Compounds as Catalyzed by a Rhodium–Diene Complex: Application to the Synthesis of (*S*)-Pregabalin and (–)-α-Kainic Acid

Chem. Eur. J. **2012**, *18*, 13274–13278.

Synthesis of Pregabalin



Further examples of adducts derived from the asymmetric conjugate addition reaction:



Significance: Pregabalin (Lyrica®) is a lipophilic GABA analogue that is prescribed for the treatment of epilepsy. This short, small-scale synthesis of pregabalin features a highly enantioselective asymmetric conjugate addition of the alkenyl trifluoroborate **B** to the α,β-unsaturated lactam **A** catalyzed by a rhodium complex incorporating the chiral bicyclo[3.3.0]octa-2,5-diene ligand **L**.

Comment: A further 17 examples of this new variant of the Hayashi–Miyaura asymmetric conjugate addition reaction are reported using six α,β-unsaturated carbonyl substrates and ten alkenyl trifluoroborates. The asymmetric conjugate addition was also applied to the synthesis of the potent neuroexcitatory agent α-kainic acid (seven steps, 40% overall yield).

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Synfacts 2013, 9(1), 0012 Published online: 17.12.2012
DOI: 10.1055/s-0032-1317717; **Reg-No.:** K09012SF

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