

pregabalin

kainic acid

Hayashi–Miyaura asymmetric conjugate addition

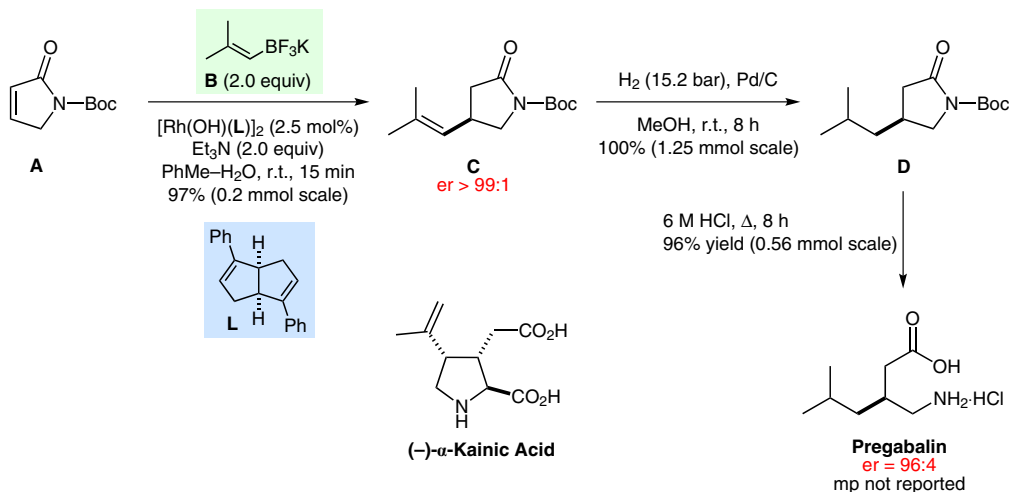
rhodium catalysis

alkenyl trifluoroborates

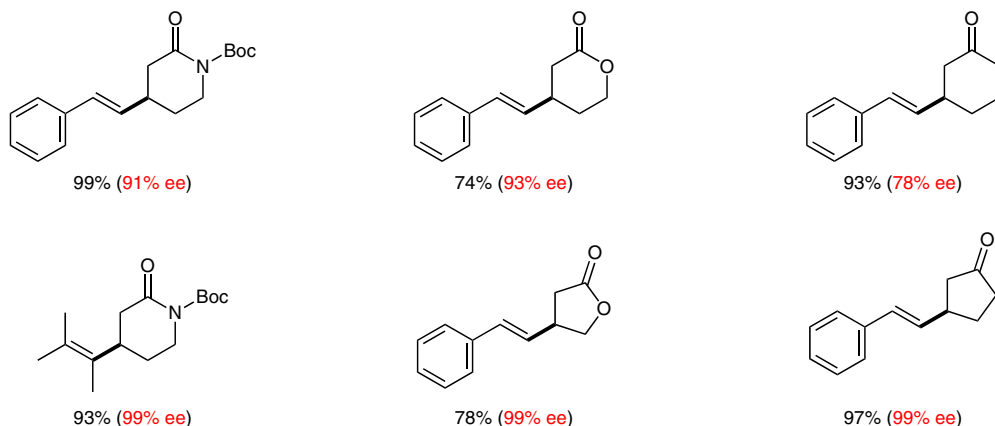
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Highly Enantioselective Alkenylation of Cyclic α,β -Unsaturated Carbonyl Compounds as Catalyzed by a Rhodium–Diene Complex: Application to the Synthesis of (*S*)-Pregabalin and (–)- α -Kainic Acid
Chem. Eur. J. **2012**, *18*, 13274–13278.

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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