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

Synthesis of Pregabalin

**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).

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

99% (91% ee) 74% (93% ee) 93% (78% ee)
93% (99% ee) 78% (99% ee) 97% (99% ee)

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