Synthesis of Pregabalin

![Chemical Structures]

**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 \( \alpha,\beta \)-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 \( \alpha,\beta \)-unsaturated carbonyl substrates and ten alkenyl trifluoroborates. The asymmetric conjugate addition was also applied to the synthesis of the potent neuroexcitatory agent \( \alpha \)-kainic acid (seven steps, 40% overall yield).