Synthesis of a Precursor to LY2140023

**Significance:** LY2140023 is a conformationally restricted glutamic acid analogue that is an mGlu2/3 receptor agonist. It entered phase II clinical trials for the treatment of schizophrenia. The following synthesis was used to deliver over one metric ton of the key intermediate K.

**Comment:** Whilst the later steps are described on large scale, the earlier steps, especially the critical carbene insertion reaction leading to cyclopropane B, is reported on a small scale. A large-scale (206 mol) hydroboration of B using BH$_3$-THF complex is described.

**Key words:** LY2140023, mGlu2/3 receptor agonist, cyclopropanation, Bucherer-Bergs reaction

**Category:** Synthesis of Natural Products and Potential Drugs