M. WASER,* E. D. MOHER ET AL.* (DSM FINE CHEMICALS AUSTRIA NFG GMBH & CO KG, LINZ, AUSTRIA AND ELI LILLY AND COMPANY, INDIANAPOLIS, USA)

Process Development for a Key Synthetic Intermediate of LY2140023, a Clinical Candidate for the Treatment of Schizophrenia

Org. Process Res. Dev. 2011, 15, 1266-1274.

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**.

SYNFACTS Contributors: Philip Kocienski Synfacts 2012, 8(2), 0121 Published online: 19.01.2012 **DOI:** 10.1055/s-0031-1289963; **Reg-No.:** K07611SF **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 BH₃·THF complex is described.

Category

Synthesis of Natural Products and Potential Drugs

Key words

LY2140023

mGlu2/3 receptor agonist

cyclopropanation

Bucherer-Bergs reaction

