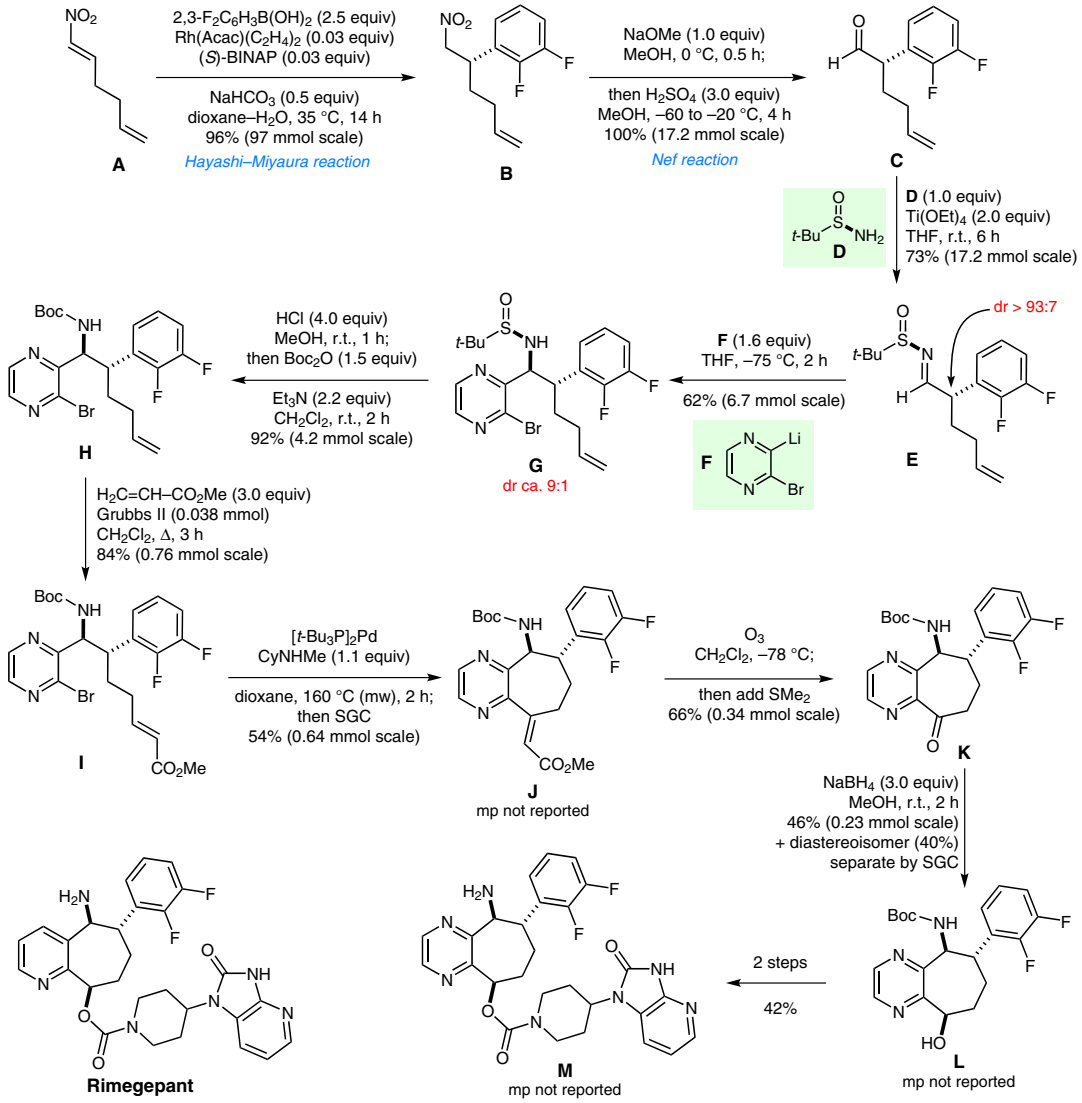
G. LUO,* L. CHEN, C. M. CONWAY, W. KOSTICH, J. E. MACOR, G. M. DUBOWCHIK
(BRISTOL-MYERS SQUIBB RESEARCH AND DEVELOPMENT, WALLINGFORD, USA)
Asymmetric Synthesis of Heterocyclic Analogues of a CGRP Receptor Antagonist for Treating Migraine
Org. Lett. **2015**, *17*, 5982–5985.

Synthesis of a CGRP Receptor Antagonist



Significance: The target molecule **M** is a calcitonin gene-related peptide (CGRP) receptor antagonist that is of interest for the treatment of migraine. It is one of four analogues of rimegepant that were prepared by a common strategy featuring the use of a Hayashi–Miyaura asymmetric conjugate addition (**A** → **B**) and Ellman–Davis protocol (**E** → **G**) to set two of the three stereogenic centers.

Comment: Attempts to construct the seven-membered ring from **I** by an intramolecular Heck reaction were thwarted by the rearrangement of the exocyclic alkene product to a trisubstituted alkene. This alkene isomerization was suppressed in part by addition of an ester group in **J**.

SYNFACTS Contributors: Philip Kocienski
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Category

Synthesis of Natural Products and Potential Drugs

Key words

CGRP receptor antagonist

Hayashi–Miyaura reaction

asymmetric conjugate addition

intramolecular Heck reaction

Ellman–Davis amine synthesis