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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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

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**Key words**

CGRP receptor antagonist

Hayashi–Miyaura reaction

asymmetric conjugate addition

intramolecular Heck reaction

Ellman–Davis amine synthesis