Synthesis of Verubecestat

Significance: Verubecestat (MK-8931) is a β -secretase inhibitor that is of interest for the treatment of Alzheimer's disease. The key step in the μmol -scale synthesis depicted is the construction of the aza-quaternary center in fragment **D** through a palladium-catalyzed, enantioselective addition of arylboronic acid **B** to cyclic imino-sulfate **A**. The desired cyclic sulfaminate **D** was obtained in 90% yield and 99% ee.

Comment: The scope of the palladium-catalyzed enantioselective arylation reaction was explored using seven cyclic iminosulfates and eleven arylboronic acids. The reaction tolerates electron-rich, electron-poor, and *ortho*-substituted arylboronic acids and provides cyclic sulfamates in high yields with excellent enantioselectivities. This palladium catalyst system significantly expands the scope for the asymmetric arylation of ketimines.

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