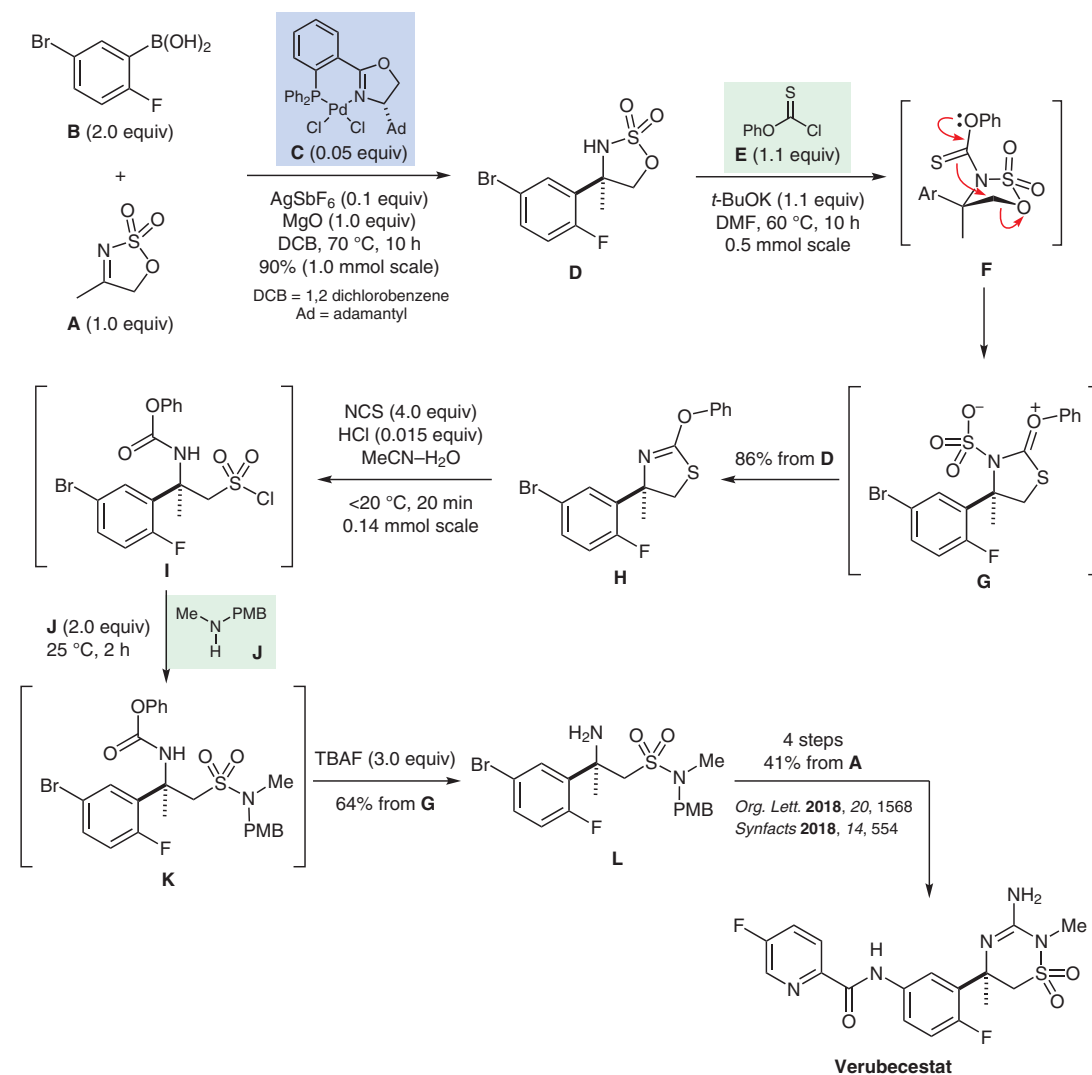


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 Palladium-Catalyzed Enantioselective Synthesis of Cyclic Sulfamidates and Application to a Synthesis of Verubecestat  
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## Synthesis of Verubecestat



**Significance:** Verubecestat (MK-8931) is a  $\beta$ -secretase inhibitor that is of interest for the treatment of Alzheimer's disease. The key step in the  $\mu$ mol-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 sulfamidate **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 sulfamidates in high yields with excellent enantioselectivities. This palladium catalyst system significantly expands the scope for the asymmetric arylation of ketimines.

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