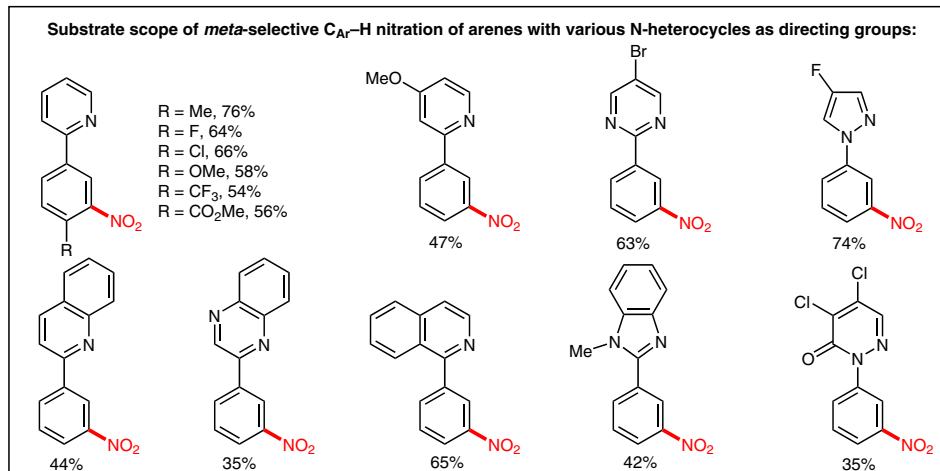
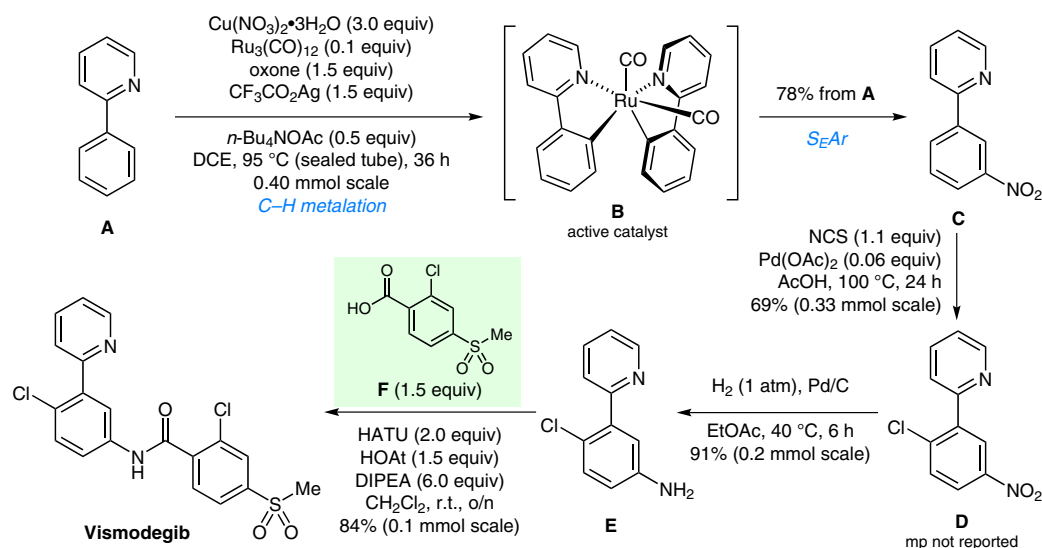


## Synthesis of Vismodegib through *meta*-Selective Nitration of Arenes



**Significance:** Zhang and co-workers report the first example of a *meta*-selective C<sub>Ar</sub>-H nitration of arenes bearing diverse N-heterocycles as directing groups. The reaction employs Ru<sub>3</sub>(CO)<sub>12</sub> as the catalyst and Cu(NO<sub>3</sub>)<sub>2</sub> as the nitrating agent. The postulated 18-electron octahedral intermediate **B** was synthesized and characterized by X-ray crystallography. Complex **B** reacted with Cu(NO<sub>3</sub>)<sub>2</sub> to give nitroarene **C** in 70% yield.

**SYNFACTS Contributors:** Philip Kocienski  
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**Comment:** A synthesis of hedgehog inhibitor vismodegib depicted together with a further 32 examples of various N-heterocyclic directing groups establish the broad scope of the reaction. Note the use of a palladium-catalyzed, heteroatom-directed *ortho* metalation of nitroarene **C**. For a strategically related synthesis of vismodegib featuring a ruthenium-catalyzed *meta* bromination, see: Q. Yu, L. Hu, Y. Wang, S. Zheng, J. Huang *Angew. Chem. Int. Ed.* **2015**, *54*, 15284.