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>2</sub>)<sub>2</sub> to give nitroarene C in 70% yield.

**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 metatization 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.