Ring Opening of Azabicyclic Alkenes Co-Catalyzed by Palladium and Copper

Significance: The ring opening of strained meso-heterobicyclic alkenes with different nucleophiles serves as a useful strategy for setting multiple stereocenters in a single transformation. Previous methods for this particular ring opening were limited to the use of bulky terminal acetylenes. Here, the authors report the development of a palladium and copper co-catalyzed system that exhibits broad substrate scope.

Comment: The authors propose that the copper(II) catalyst plays two distinct roles in the mechanism: (1) Copper facilitates transmetalation of the acetylene to palladium via the copper acetylide; (2) Copper behaves as a Lewis acid to activate the azabicyclic alkene. In addition to demonstrating wide functional group tolerance, the yields and enantioselectivities observed are excellent across the series of substrates tested.

Selected examples:
- NHBoc Ph: 97% yield, 97% ee
- NHBoc TES: 98% yield, 95% ee
- NHBoc Ph: 89% yield, 94% ee
- NHBoc Ph: 82% yield, 96% ee