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(I) 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.

**Proposed mechanism:**

\[
\begin{align*}
\text{1} & \quad \text{1.0 equiv} \\
\text{2} & \quad \text{5.0 equiv}
\end{align*}
\]

\[
Pd(OAc)_2 (5 \text{ mol\%}) + \text{(R)-xyl-BINAP} (6 \text{ mol\%}) + CuOTf (10 \text{ mol\%}) \quad \text{DME, 0 °C}
\]

**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

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