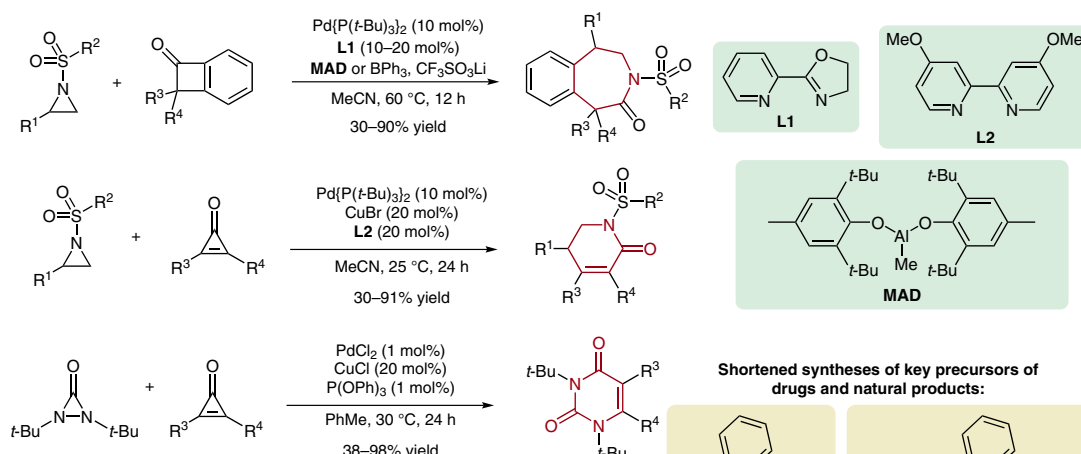
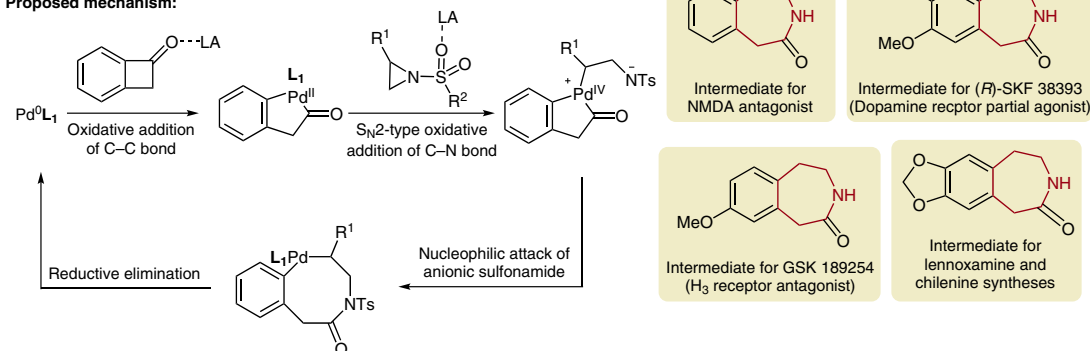


Aziridines Cross-Dimerize to Larger N-Heterocycles

Cross-dimerization of aziridines and diaziridinones:



Proposed mechanism:



Significance: Azepines, dihydropyridinone, and uracil are key N-heterocyclic motifs found in numerous drug molecules. However, syntheses of these rings often require multistep routes and suffer from poor efficiency. The authors present a robust catalytic method to access these azaheterocycles in an enantiospecific manner via cross-dimerization of aziridines or diaziridinones with cyclopropanones or cyclobutenones. This ring-expansion strategy enabled step-efficient syntheses of several pharmaceutical agents and natural products, underpinning the broader synthetic utility.

Comment: Lewis acid-mediated, Pd-catalyzed cross-dimerization of sulfonlated aziridines to benzacyclobutanone afforded the benzazepine skeleton. A synergistic Pd-Cu catalyst system was used to access the pyridinone and uracil motifs from cyclopropanone. A mechanistic study revealed a Pd^{0/III/IV} cycle starting with an oxidative C–C cleavage of the strained carbocycle followed by oxidative aziridine opening to form a Pd^{IV} intermediate, which was supported by computational models. This protocol provided concise routes to useful drug precursors (e.g. SKF 38393, GSK 189254, ivabradine) with further synthetic modifications of the azepines, rendering this a potential retrosynthetic tool.