R. LI, B. LI, H. ZHANG, C.-W. JU, Y. QIN, X.-S. XUE, D. ZHAO\* (NANKAI UNIVERSITY, TIANJIN, P. R. OF CHINA)

A Ring Expansion Strategy towards Diverse Azaheterocycles *Nat. Chem.* **2021**, DOI: 10.1038/s41557-021-00746-7.

## **Aziridines Cross-Dimerize to Larger N-Heterocycles**

## Cross-dimerization of aziridines and diaziridinones:

**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 cyclopropenones 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 sulfonylated aziridines to benzacyclobutanone afforded the benzazepine skeleton. A synergistic Pd-Cu catalyst system was used to access the pyridinone and uracil motifs from cyclopropenone. A mechanistic study revealed a Pd<sup>0/III/IV</sup> cycle starting with an oxidative C–C cleavage of the strained carbocycle followed by oxidative aziridine opening to form a Pd<sup>IV</sup> 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.

**SYNFACTS Contributors:** Dirk Trauner, Tufan K. Mukhopadhyay Synfacts 2021, 17(10), 1147 Published online: 17.09.2021 **DOI:** 10.1055/s-0040-1720203; **Reg-No.:** T08421SF

Chemistry in Medicine and Biology

## Key words

aziridine crossdimerization

Pd-catalyzed ring expansion

azepine

uracil

