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Rhodium-Catalyzed One-Carbon Ring Expansion of Aziridines with Vinyl-*N*-triftosylhydrazones for the Synthesis of 2-Vinyl Azetidines

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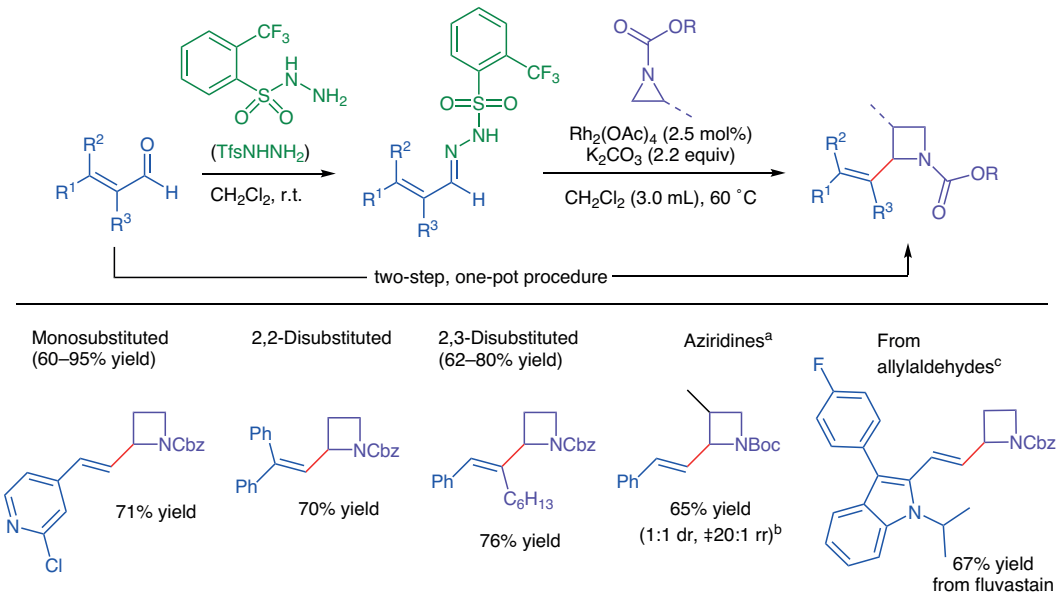
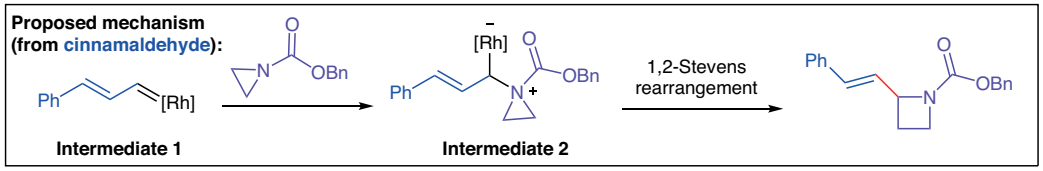
Rhodium-Catalyzed One-Carbon Ring Expansion of Aziridines for the Synthesis of 2-Vinyl Azetidines



[a] Common carbamate protecting groups gave good yields (83–95%); Fmoc not studied.
[b] Diastereoselectivity and regioisomeric ratio determined by ^{1}H NMR analysis of the crude product.
[c] Late-stage modification of molecules bearing an allylaldehyde moiety.



Significance: Methodologies for the ring expansion of aziridines are useful for accessing structural motifs that are not easily incorporated onto azetidines. This protocol utilizes the strain within the aziridine to drive the reaction forward in contrast to strain-inducing cyclization, which may be unfavorable/not observed. The introduction of the double bond provides an additional handle from which further transformations are possible. Late-stage modification of drug candidates allows for rapid expansion of the scope of structure–activity relationship studies (SARs).

Comment: This two-step protocol can be accomplished in one reaction vessel without the need for isolation of the intermediate. No cheletropic extrusion products were observed. Highly regioselective stereocontrol may be possible with the use of chiral ligands. Experimental and computational studies indicate this transformation proceeds via a diradical mechanism.

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Category
Synthesis of Heterocycles

Key words
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