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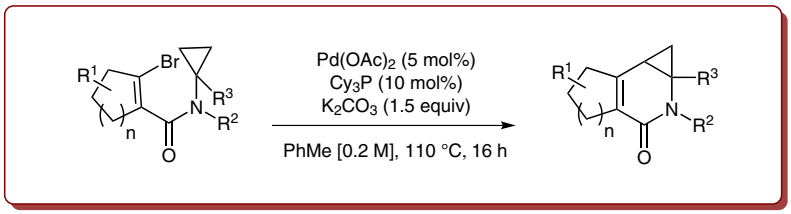
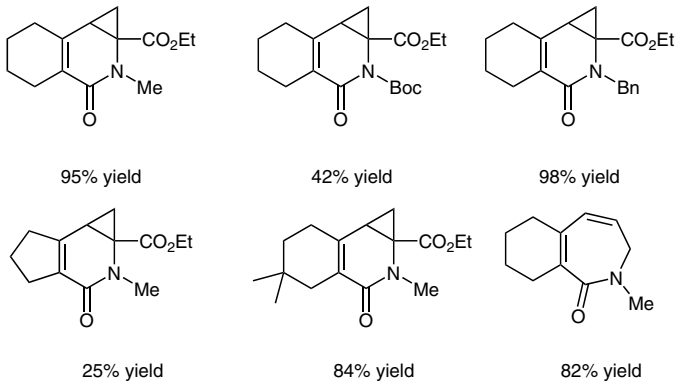
C. L. LADD, A. B. CHARETTE* (UNIVERSITÉ DE MONTREAL, CANADA)
Access to Cyclopropyl-Fused Azacycles via a Palladium-Catalyzed Direct Alkenylation Strategy
Org. Lett. **2016**, *18*, 6046–6049.

Palladium-Catalyzed Synthesis of Cyclopropyl-Fused Azacycles



Representative examples:



Significance: Building on their earlier studies on C–H arylation of cyclopropanes (*Org. Lett*. **2013**, *15*, 1350), Ladd and Charette report a palladium-catalyzed cyclization strategy for intramolecular cyclopropyl alkenylation. The substrates for the reaction are easily accessible through amidation of cyclopropyl amines with the corresponding carboxylic acid derivatives. Although the scope of the method is somewhat narrow with regard to the alkene component, the ability to use removable protecting groups (such as Boc or PMB) on the amide makes the products more versatile and amenable to further functionalization. Also reported is an enantioselective variant of the strategy that uses Feringa's BINOL phosphoramidite ligand.

Comment: The optimized reaction conditions worked fairly well across the range of reported substrates; for low-yielding reactions, the efficiency was improved by the addition of pivalic acid. The method is ideally suited for cyclohexenyl bromide derivatives. Although there is one reported example of a cyclopentene substrate, rings with more than six members did not undergo the desired cyclization. Additionally, no reaction was observed when the cyclopropyl moiety was replaced with an sp^3 system. Further modification of the cyclopropyl ring of the products can be envisaged. Interestingly, in the absence of an α-substituent on the cyclopropane, the ring-opened dihydroazepinone product was formed exclusively and in good yield.

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