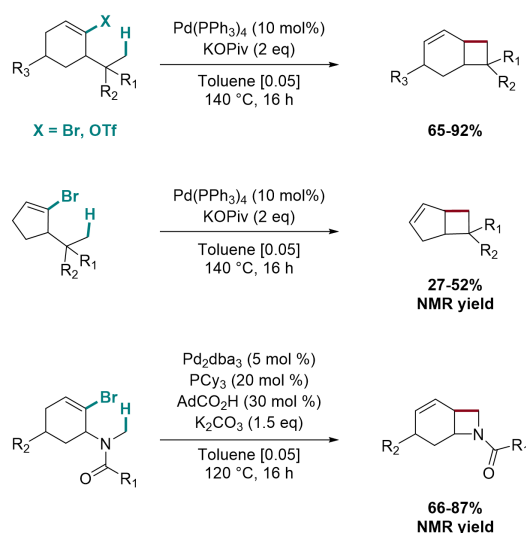


Construction of 4-membered rings through an intramolecular C(sp³)-H activationM. Tsitopoulou¹, A. Clemenceau¹, P. Thesmar¹, O. Baudoin^{1*}¹Department of Chemistry, University of Basel

1,4-Palladium shift has been established as an elegant approach towards the functionalization of remote C-H bonds.^{1,2} However, its application is restricted to using aryl halides as precursors.³⁻⁵ In this work, we have successfully extended its application to C(sp²)-X alkenyl precursors. As a result, we report an unprecedented cyclobutanation protocol towards fused cyclobutane derivatives using alkenyl (pseudo)halides through a Pd⁰-catalyzed C(sp³)-H activation process. This reaction takes place via 1,4-Pd shift followed by intramolecular Heck coupling. The methodology performs best with cyclohexenyl precursors giving access to a variety of substituted bicyclo[4,2,0]octenes, and also shows a potential for accessing smaller ring systems starting from cyclopentenyl halides. Replacing the alkyl chain with N-methyl amides gives access to fused azetidines via the same mechanism. Early kinetic studies indicate a primary kinetic isotope effect establishing the C-H activation as the rate-determining step, while deuterium incorporation suggests an irreversible 1,4-Pd shift process, – probably arising from the fast trapping of the σ -alkylpalladium species through Heck coupling.

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