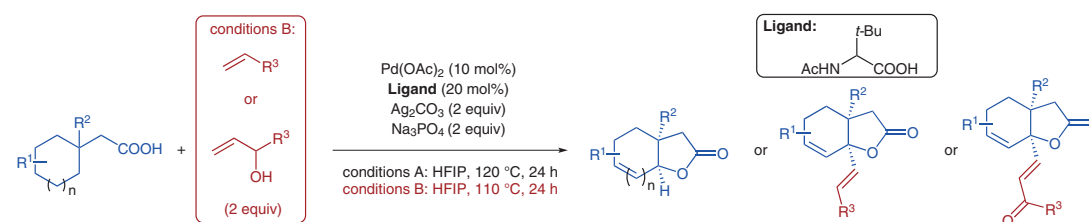


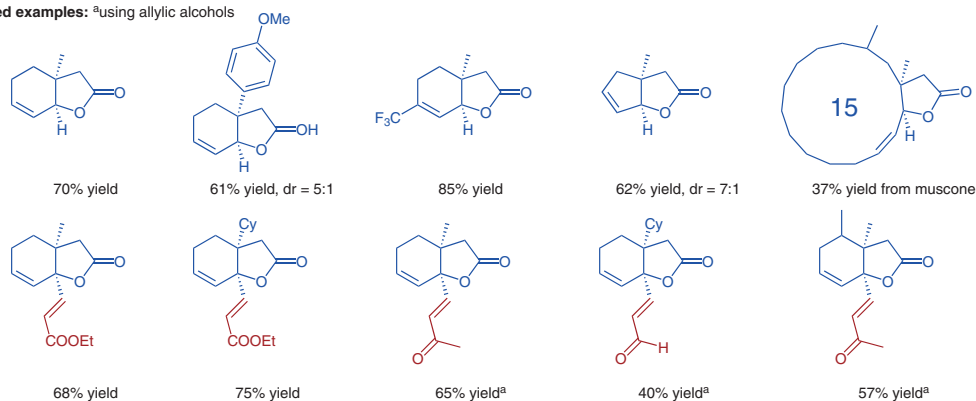
J. DAS, W. ALI, A. GHOSH, T. PAL, A. MANDAL, C. TEJA, S. DUTTA, R. POTHIKUMAR, H. GE*, X. ZHANG*, D. MAITI* (TEXAS TECH UNIVERSITY, LUBBOCK, USA; AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH (A*STAR), SINGAPORE; INDIAN INSTITUTE OF TECHNOLOGY BOMBAY, MUMBAI, INDIA)

Access to Unsaturated Bicyclic Lactones by Overriding Conventional C(sp³)-H Site Selectivity
Nat. Chem. **2023**, *15*, 1626–1635, DOI: 10.1038/s41557-023-01295-x.

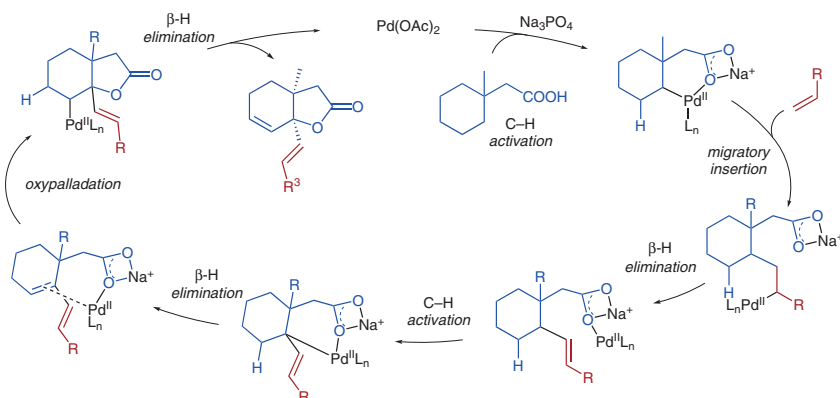
Regioselective C(sp³)-H Activation of Cyclic Aliphatic Acids: Synthesis of Unsaturated Bicyclic Lactones



Selected examples: ^ausing allylic alcohols



Proposed mechanism: intermolecular C-H activation/Heck/olefination reaction



Significance: Maiti, Zhang, Ge and co-workers report a selective γ -methylene C-H activation in the presence of γ -methyl groups. The subsequent β -H elimination/oxypalladation/ β -H elimination cascade furnishes fused unsaturated lactones, which are commonly encountered in natural products. In the presence of an exogenous alkene or allylic alcohol, a quaternary stereocenter can be generated.

Comment: DFT calculations suggest that although the mono-protected amino acid (MPAA) assisted C-H activation of the methyl C(sp³)-H bond is 3.4 kcal mol⁻¹ lower than that of the methylene group, the subsequent reductive elimination to the corresponding spirocycle has a very high barrier of 45.3 kcal mol⁻¹, making the methylene C(sp³)-H activation pathway more favorable.

SYNFACTS Contributors: Mark Lautens, Jonathan Bajohr
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