R. ZHANG, T. YU, G. DONG* (UNIVERSITY OF CHICAGO, USA)
Rhodium Catalyzed Tunable Amide Homologation through a Hook-and-Slide Strategy
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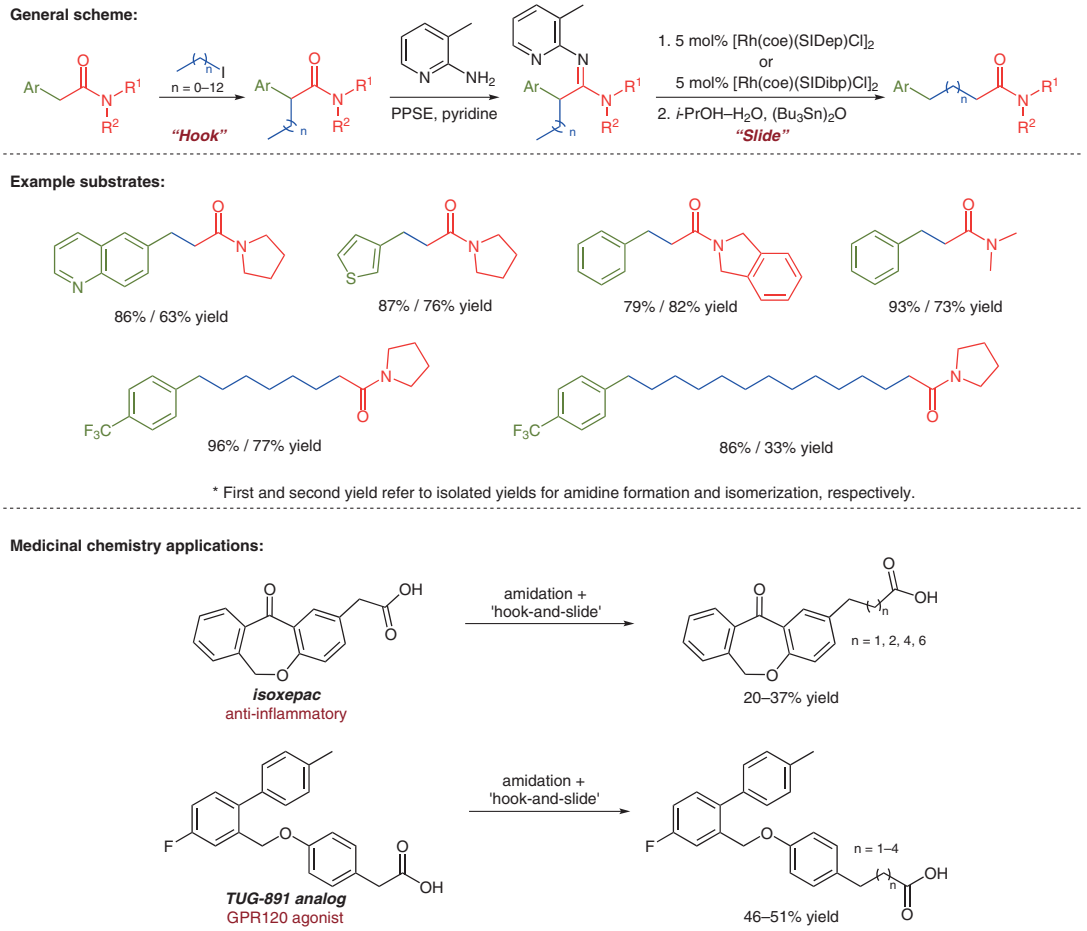
A Rhodium-Catalyzed "Hook-and-Slide" Homologation of Amides



Significance: Functional group homologation represents a powerful strategy in medicinal chemistry, enabling late-stage access to drug homologs with potentially significantly different bioactivities to the parent compound. Given the prevalence of amides in medicinal chemistry and dearth of available methods, new methods for amide homologation are particularly needed. In this work, Dong and co-workers present a 'hook-and-slide' strategy for amide homologation involving α-alkylation, amidine formation, rhodium-catalyzed branched-to-linear isomerization, and directing group removal.

Comment: The hook-and-slide strategy, while requiring an aromatic substituent in the α-position of the amide, is amenable to a variety of homologation lengths and substituents on the amide nitrogen. Incorporating an amidation step in the sequence and altering the conditions for the directing group removal allowed for the homologation of carboxylic acids as well. This strategy was utilized for creation of homologs of the anti-inflammatory drug isoxepac and the GPR120 agonist TUG-891.

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