



Transfer Hydrogenation of Pyridinium and Quinolinium Species Using Ethanol as a Hydrogen Source

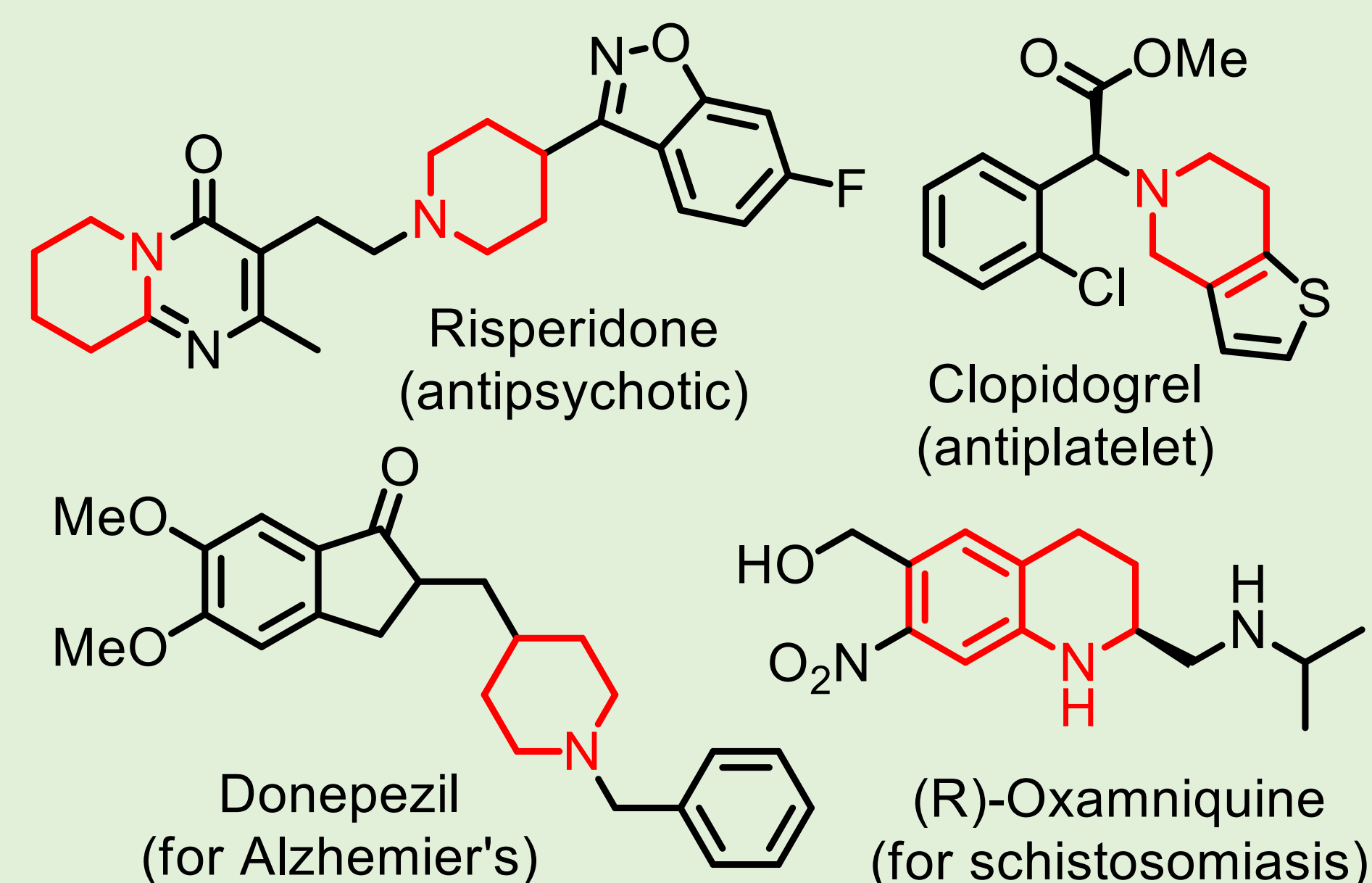
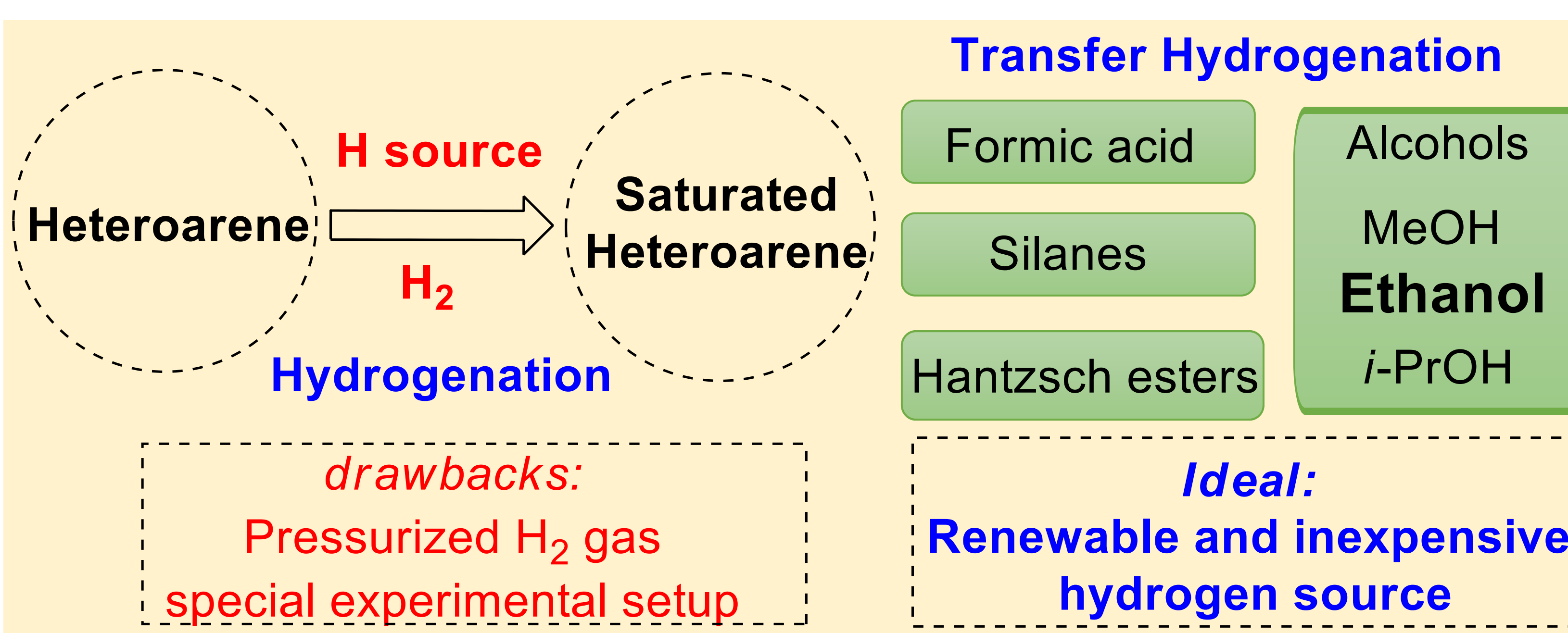
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ABSTRACT: Catalytic transfer hydrogenation (TH) for the reduction of heterocycles is an emerging powerful strategy for accessing biologically active saturated N-heterocycles as it employs readily available, inexpensive, and easy-to-handle hydrogen donors. However, the use of the most abundant renewable feedstock, ethanol, as a hydrogen source in the reduction of heterocycles, remains in its infancy, largely due to the formation of catalytically inactive metal carbonyl species and the high energy barrier of dearomatization. Described herein is a TH protocol that utilizes ethanol as a hydrogen source and an Ir catalyst for the reduction of quinolines and pyridines to tetrahydroquinolines and piperidines, respectively.

Representative drugs & biologically active substrates



Transfer Hydrogenation of azines using EtOH as a hydrogen source: Challenges

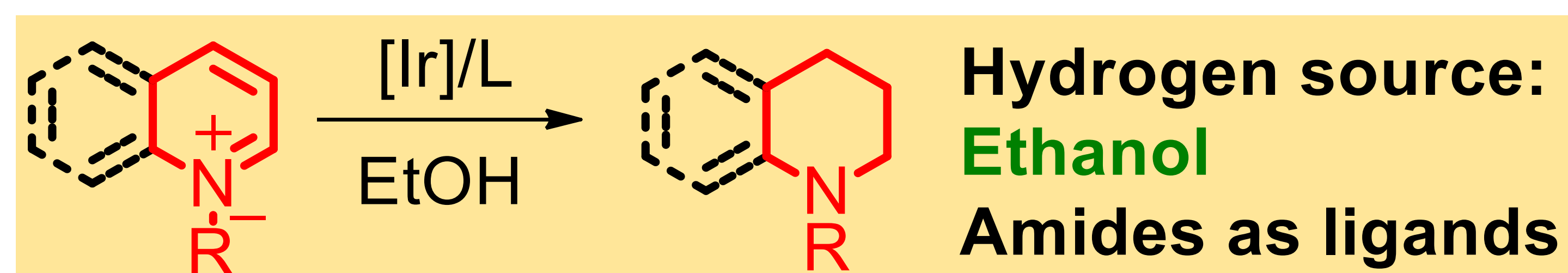
Possible catalyst deactivation with EtOH by forming metal-carbonyl species

High energy barrier dearomatization of resonance stabilized heterocycles

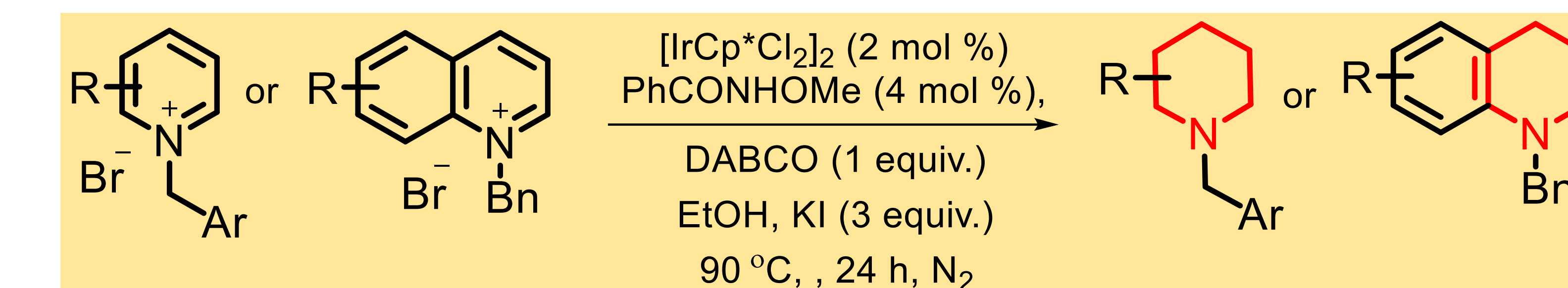
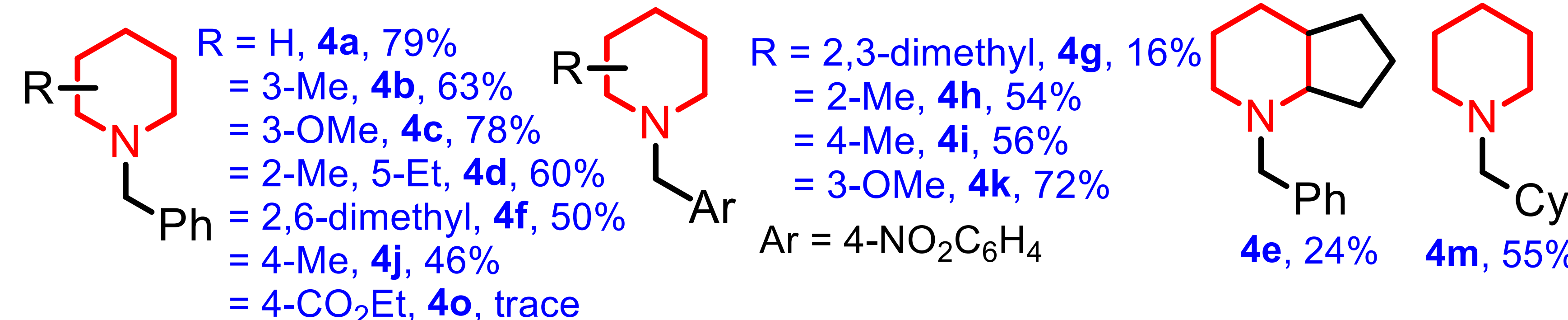
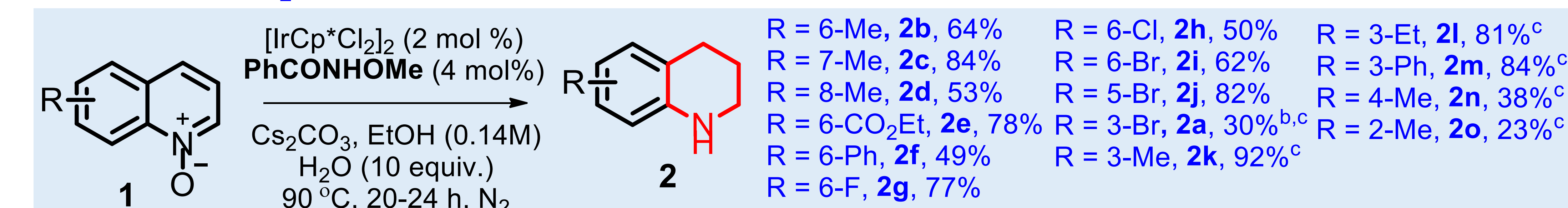
Previous work



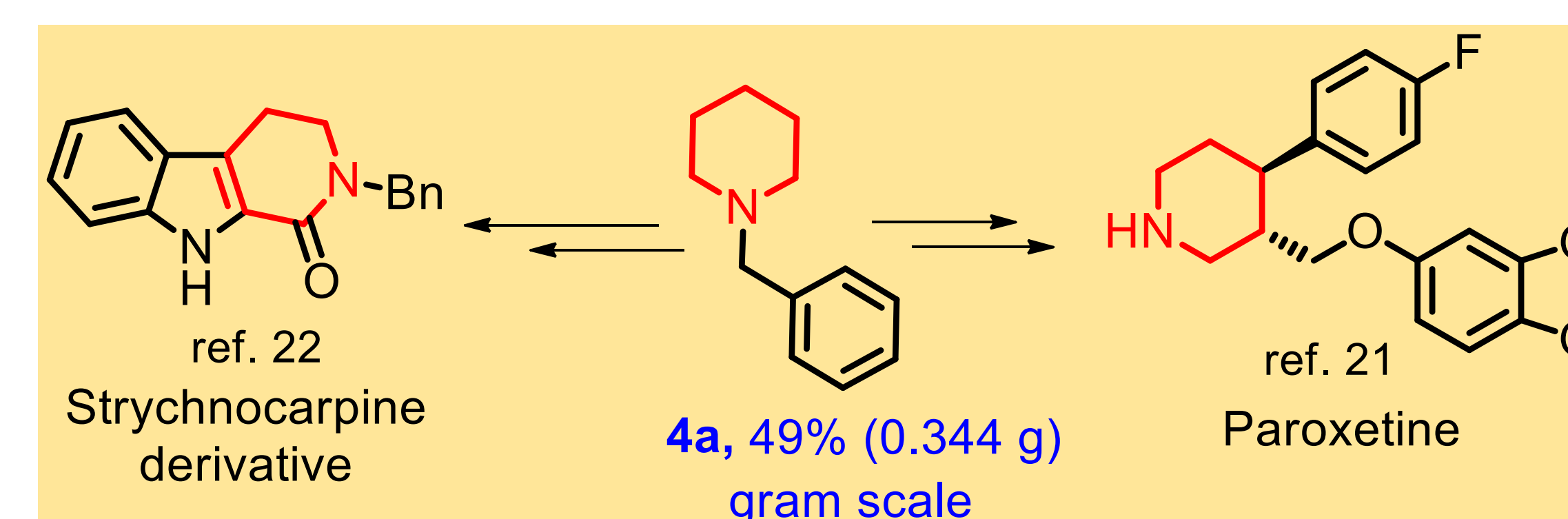
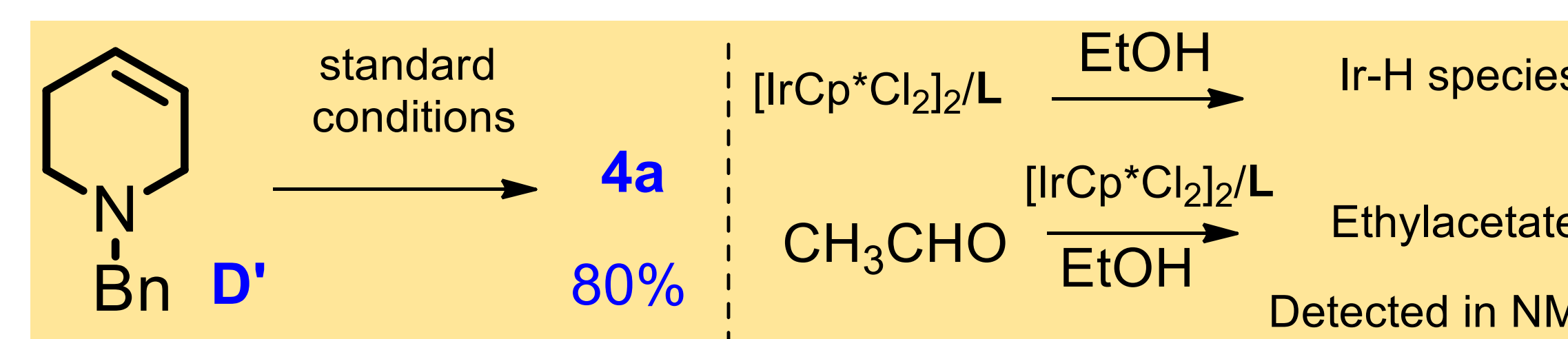
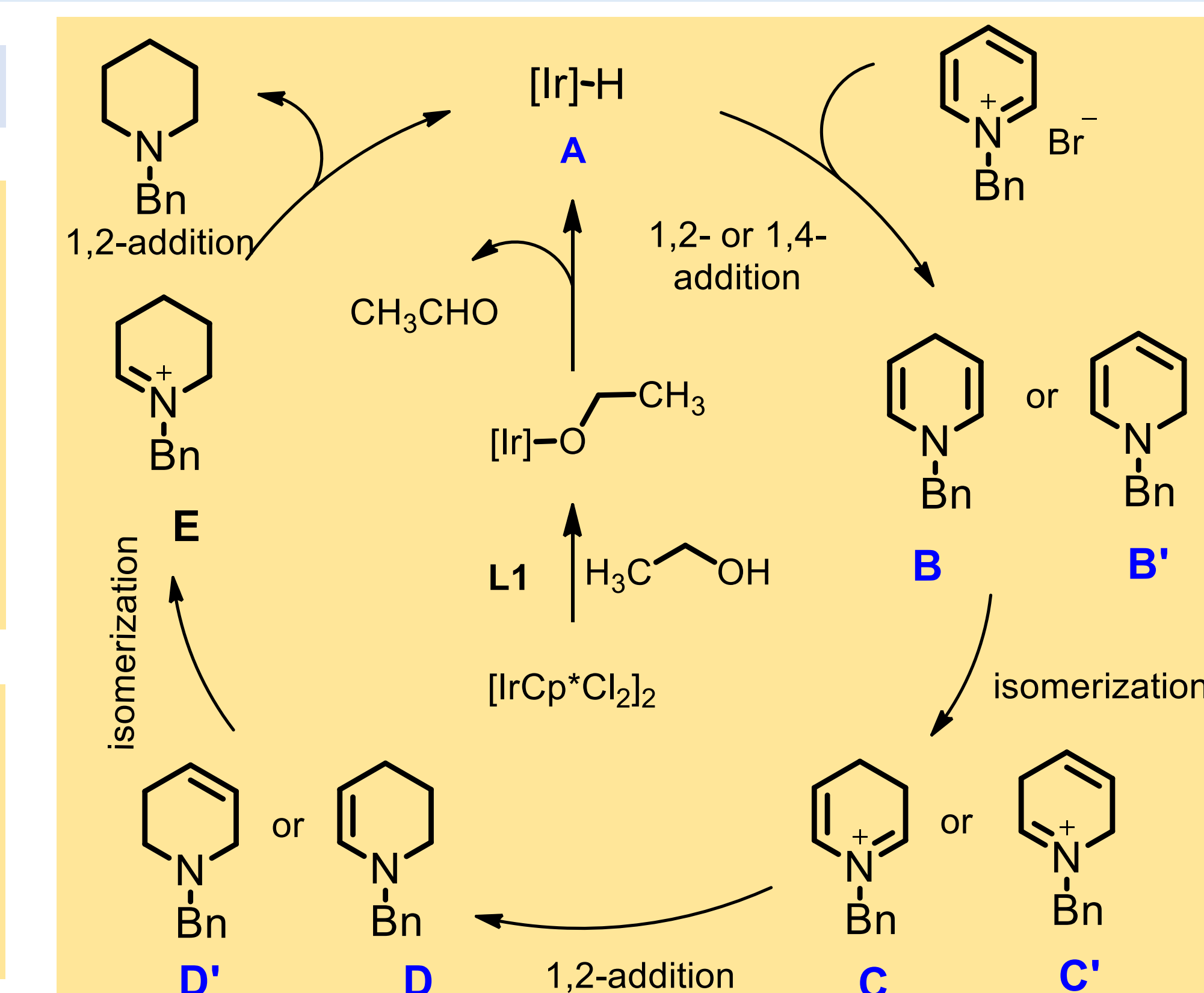
This work: TH of pyridinium and quinolinium salts



Optimized Reaction Conditions and substrate scope



Synthetic Transformations and Mechanism



- Ethanol as a hydrogen source to access tetrahydroquinoline and piperidine derivatives. Readily available amides were used as ligands for the first time.
- We believe that this study may inspire the development of sustainable and efficient protocols using the most abundantly available feedstock, ethanol.

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