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Rhodium(II)-Catalyzed Asymmetric Intermolecular C(sp³)-H Amination

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The nitrogen atom is of prime importance in life sciences, as highlighted by its presence in many natural products. More significantly, nitrogen can be found in a myriad of agrochemicals and pharmaceuticals (Figure 1). A recent study has indeed revealed that 84% of the FDA approved drugs contain at least one nitrogen atom.¹ Such ubiquity can be rationalized by the ability of nitrogen to tune the pharmacokinetic and pharmacodynamic properties of a bioactive compound.

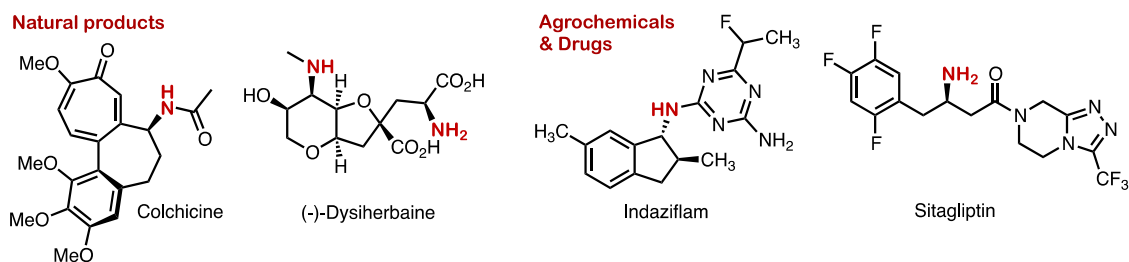
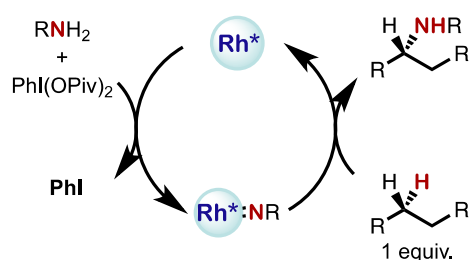


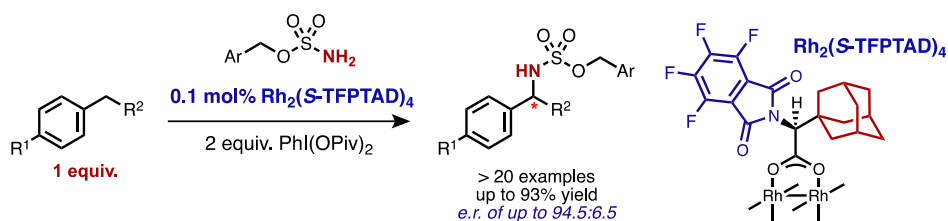
Figure 1. Examples on nitrogen-containing natural products, drugs and agrochemicals

The importance of nitrogen has translated into the development of several C-N bond forming reactions. Among these methods, the application of catalytic nitrene additions has culminated in the discovery of efficient transformations for the direct amination of C(sp³)-H bonds. Synthetically useful methods have particularly been reported through the combination of hypervalent iodine chemistry and dirhodium(II) catalysis (Scheme 1).² They allow for functionalizing efficiently hydrocarbons in an intra- or an intermolecular manner.



Scheme 1. Rhodium(II)-catalyzed C(sp³)-H amination

Catalytic asymmetric C(sp³)-H amination reactions have also been reported for the formation of enantiopure amines,³ however, despite significant achievements, the catalytic enantioselective intermolecular reaction remains a challenging issue to address. In this communication, we will thus discuss the results of our investigations in this context that are based on the design of new nitrene sources and chiral dirhodium(II) complexes (Scheme 2).⁴



Scheme 2. Catalytic asymmetric intermolecular C(sp³)-H amination

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