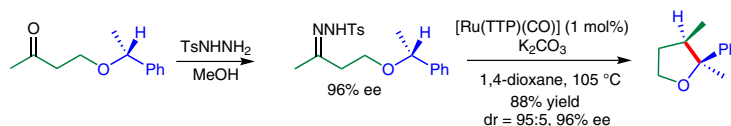
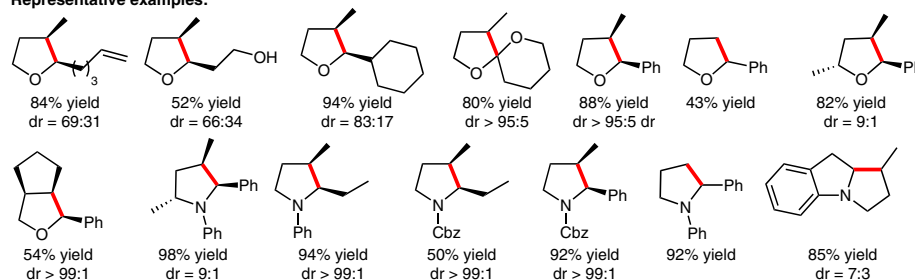


A. R. REDDY, C.-Y. ZHOU, Z. GUO, J. WEI, C.-M. CHE* (HKU SHENZHEN INSTITUTE OF RESEARCH AND INNOVATION AND THE UNIVERSITY OF HONG KONG, P. R. OF CHINA) Ruthenium–Porphyrin-Catalyzed Diastereoselective Intramolecular Alkyl Carbene Insertion into C–H Bonds of Alkyl Diazomethanes Generated In Situ from *N*-Tosylhydrazones
Angew. Chem. Int. Ed. **2014**, *53*, 14175–14180.

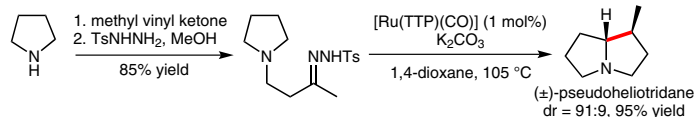
Tetrahydrofurans and Pyrrolidines from *N*-Tosylhydrazones via C–H Insertion



Representative examples:



Application:



Significance: Reported is a method for synthesizing substituted tetrahydrofurans and pyrrolidines from acyclic *N*-tosylhydrazones via an intramolecular ruthenium–porphyrin catalyzed C–H insertion process. Key to the success of this method was the identification of conditions for minimizing decomposition (elimination) of the alkylcarbene or carbenoid intermediate, which was realized through careful optimization of base, solvent and catalyst. The ruthenium–porphyrin catalyst used in this study is not commercially available, but is readily prepared in a single step. A one-pot method for accessing the tetrahydrofuran or pyrrolidine products from the corresponding acyclic ketone was also reported and proceeded with comparable yields. The power of this methodology is demonstrated through a concise synthesis of the alkaloid (±)-pseudoheliotridane from pyrrolidine.

Comment: Pyrrolidines and tetrahydrofurans are two of the most prevalent heterocycles found in drugs today. The present method demonstrates good scope for accessing these heterocycles, tolerating both alkenes and free alcohols, and provides access to structurally diverse products including spiro, attached ring, and fused ring systems from easily accessible starting materials. *N*-Tosylhydrazones derived from either aldehydes or ketones were viable substrates, allowing for flexible substitution at the 3 position of the heterocycle. In those cases in which two or more stereocenters were introduced, a high level of 2,3-*cis* diastereoselectivity was observed, especially in the synthesis of pyrrolidines. Kinetic isotope effect experiments and the observed stereospecificity of the present reaction provide strong support for a concerted C–H insertion process.

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