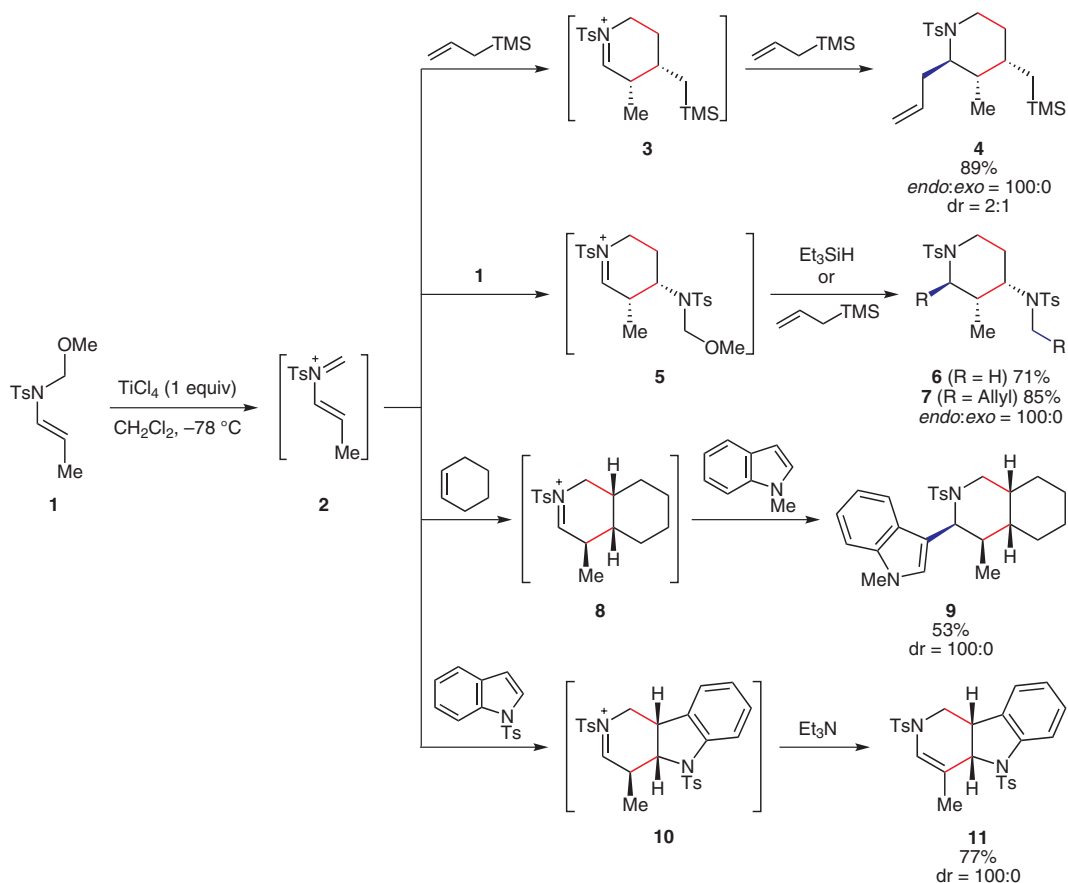


Synthesis of Polysubstituted Piperidines by Diels–Alder Reaction of *N*-Alkenyl Iminiums



Significance: The synthesis of piperidine derivatives by the [4+2] cycloaddition of *N*-alkenyl iminium ion **2** with alkene dienophiles is reported. Treatment of methoxymethyl enamine **1** with TiCl_4 gave diene **2**, which was trapped in situ with a range of alkenes to give iminium cycloadducts **3**, **5**, **8**, and **10**. Addition of a nucleophile (allyl silane, indole) afforded piperidines **4**, **6**, **7**, and **9** in excellent yield with complete *endo* selectivity. Quenching iminium salt **10** with triethylamine generated the tetrahydropyridine **11** as a single isomer.

Comment: Piperidine structural motifs are found in a large number of natural products and pharmaceuticals. The hetero-Diels–Alder reaction is a powerful method for the synthesis of this class of compound. The current method generates an iminium cycloadduct which allows for further functionalization by addition of a nucleophile to afford highly substituted piperidine derivatives in one pot from readily available starting materials.