## Synthesis of Polysubstituted Piperidines by Diels-Alder Reaction of $\boldsymbol{N}$-Alkenyl Iminiums



Significance: The synthesis of piperidine derivatives by the [4+2] cycloaddition of $N$-alkenyl iminium ion $\mathbf{2}$ with alkene dienophiles is reported. Treatment of methoxymethyl enamine $\mathbf{1}$ with $\mathrm{TiCl}_{4}$ gave diene $\mathbf{2}$, which was trapped in situ with a range of alkenes to give iminium cycloadducts $\mathbf{3}$, $\mathbf{5}, \mathbf{8}$, and $\mathbf{1 0}$. Addition of a nucleophile (allyl silane, indole) afforded piperidines 4, 6, 7, and 9 in excellent yield with complete endo selectivity. Quenching iminium salt $\mathbf{1 0}$ with triethylamine generated the tetrahydropyridine $\mathbf{1 1}$ 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.

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