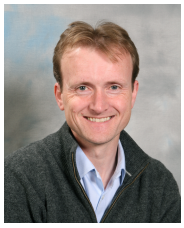

Synthesis and Reactions of Chiral Organometallics of Saturated Nitrogen Heterocycles

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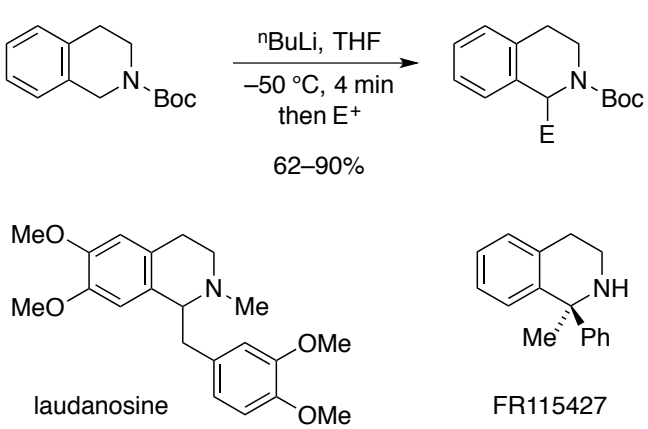
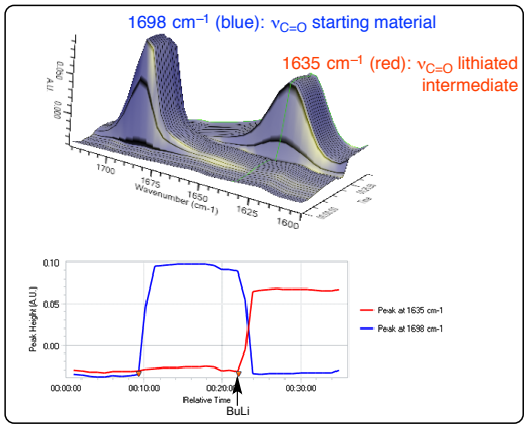
Metallation of *N*-*tert*-butoxycarbonyl (*N*-Boc) cyclic amines typically requires *sec*-BuLi and TMEDA in Et_2O at –78 °C. However, deprotonation of *N*-Boc-tetrahydroisoquinolines and 2-arylpiperidines occurs under milder conditions, with *n*-BuLi in THF at –50 °C. In fact the rate of lithiation is unsatisfactory at –78 °C due to slow rotation of the Boc group. The progress of the lithiation can be monitored by using *in situ* IR spectroscopy (see the ReactIR plots below, taken at –50 °C and showing rapid lithiation).[1]
This chemistry was used for a short synthesis of several alkaloids such as laudanosine[1] and for a preparation of the drug compound FR115427.[2]





Examples of this chemistry will be given with various saturated nitrogen-containing heterocycles.[1–4] In addition, we have discovered an efficient kinetic resolution by using *n*-BuLi and the chiral ligand sparteine.[5] Highly enantiomerically enriched *N*-Boc-2-arylpiperidines can be obtained with this resolution method.
Recently we have been investigating the configurational stability of the organometallic species formed by deprotonation of enantiopure *N*-Boc-2-cyanopiperidine.[6] The nitrile-substituted organometallics are configurationally labile but enantiomerically enriched 2,2-disubstituted piperidines can be prepared.

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